JANUARY & APRIL, 1942

JOURNAL OF NEUROLOGY AND PSYCHIATRY

CONTENTS

		Page
[illegible]	D. W. C. Northfield	1
An Experimental Approach to the Determination of Comparative Efficacy of Insulin and Convulsion Therapy	R. A. Palmer	10
The [illegible] in Neurosyphilis	A. S. Thorley	14
[illegible]	A. J. Galbraith and A. Meyer	22
[illegible] with Hypoglycæmic Coma	F. Parkes Weber and K. Blum	37
[illegible] and the Occurrence of Uræmia	J. N. Cumings	40
[illegible] Studies of Psychopathic Personalities	Denis Hill and Donald Watterson	47
[illegible]		66
[illegible]		79

PUBLISHED BY THE BRITISH MEDICAL ASSOCIATION
FOR THE PROPRIETORS AT THE BRITISH MEDICAL ASSOCIATION HOUSE,
TAVISTOCK SQUARE, W.C.1

[illegible] U.S.A. $6.00. Post Free.

Edited by

E. ARNOLD CARMICHAEL

D. DENNY-BROWN G. JEFFERSON

AUBREY LEWIS A. MEYER

R. A. McCANCE

with the assistance of the following Editorial Committee:

E. D. Adrian
W. Russell Brain
E. Bramwell
William Brown
Hugh Cairns
C. Macfie Campbell
W. E. Le Gros Clark
A. Feiling
R. A. Fisher
R. D. Gillespie
F. L. Golla
R. G. Gordon
J. G. Greenfield
Bernard Hart
R. Foster Kennedy
R. M. Stewart
C. P. Symonds
C. C. Worster-Drought
Editor of the British Medical Journal.

EDITORIAL NOTICES

THE EDITORIAL COMMITTEE will welcome original papers. They should be addressed to Dr. E. Arnold Carmichael, The National Hospital, Queen Square, W.C.1. Papers are accepted on the clear understanding that the subject matter has not been and will not be published in a separate journal.

Papers should deal with original matter and the discussion should be limited to relevant questions. Contributors should be as concise as possible and a short summary of conclusions should accompany each paper. Manuscripts should be typewritten and carefully revised, as alterations in print are costly and, apart from verbal corrections, will be charged to the contributor.

Illustrations should be prepared ready for reproduction. On the figures lettering which is written in pencil will be replaced by printer's type without charge.

References to papers in the text should be made by inserting the name of author followed by year of publication in parentheses. At the end of the paper, references should be arranged in alphabetical order of author's name. Each reference should give author's name, followed by initials and year of publication in parentheses. The name of the journal in which the article appeared should follow and should be abbreviated according to the World List of Scientific Periodicals. The volume number should be given next in arabic numerals, followed by number of first page of article.

Brown, A. B. (1885). *Rev. Neurol.*, **162**, 427.

Reprints. Fifty reprints will be given to the author or divided among the authors of a contribution; further reprints may be obtained by application to the Secretary of the Editorial Board, B.M.A. House, Tavistock Square, but notice must be given when the proof is returned.

Subscription 25/- net per annum, post free.

Applications for advertisement space should be directed to the Advertisement Manager and business communications should be addressed to the Secretary of the Journal Board.

BRITISH MEDICAL ASSOCIATION,

B.M.A. House, Tavistock Square, London, W.C.1.

THE JOURNAL OF
NEUROLOGY AND PSYCHIATRY
FOUNDED BY S. A. K. WILSON

VOL. 5. [New Series] JANUARY–APRIL, 1942 NOS. 1 & 2.

THE TREATMENT OF BRAIN ABSCESS

BY

D. W. C. NORTHFIELD

(RECEIVED 19TH FEBRUARY, 1942)

THIS review of a personal experience of the management of cases of brain abscess during the last five years is based upon 31 cases. Although 17 died, there has been a steady improvement in results, due in part to an increasing experience, and to a more mature judgment, for in no other branch of neurosurgery is an unremitting personal attention to details more essential for success. Much of the improvement, however, is due to a complete change in the fundamental method of treatment, namely, from drainage to the closed method of Clovis Vincent.

In 1936 there were two cases: the abscess was drained in each, and both died. In 1927 all of four cases were treated by drainage and only one lived. There were seven cases in 1938: in four, the abscess was drained and three of these died; in the other three the abscess was aspirated and in one of these a decompression was also performed—all of these three cases recovered. During that year I was impressed by the value of aspiration and I decided to employ it more frequently. Drainage was practically abandoned, for during the remaining period under review it was used in only two cases; one of these died, and in the other aspiration and a subtemporal decompression preceded drainage and the patient recovered. In 1939 there were nine cases, treated by various closed methods and by drainage in one case, and four lived. Four out of five cases recovered in 1940, and in 1941 two of four cases have lived.

In the following analysis are set out the various procedures and their results:

12 *Cases Drained:*	3 *Lived* (25%)
5 cases; drainage alone	1 lived
3 cases; aspiration+drainage	1 lived
1 case; decompression+drainage	0 lived
3 cases; aspiration+decompression+drainage	1 lived

19 *Cases—not Drained:*	11 *Lived* (58%)
6 cases; aspiration alone	3 lived
5 cases; decompression+aspiration	1 lived
(One death from epilepsy while awaiting enucleation.)	
2 cases; aspiration+enucleation	2 lived
5 cases; decompression+aspiration+enucleation	4 lived
1 case; enucleation alone	1 lived

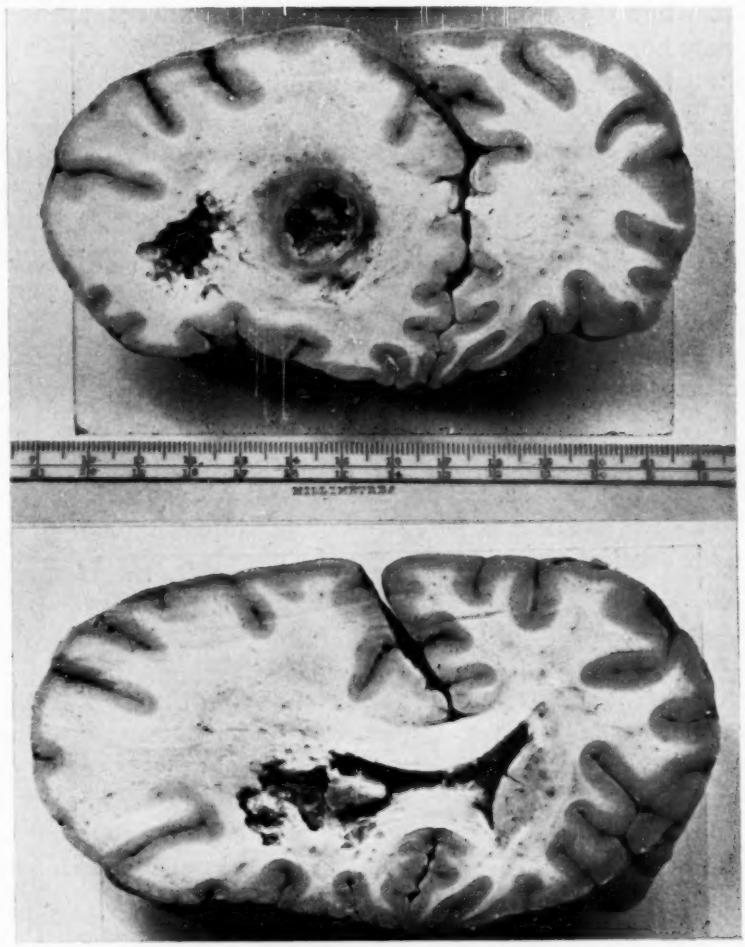
Various methods of draining an abscess were employed in the first series, by catheter, by " uncapping " and packing the cavity, by two-stage operation, and by marsupialization. The results can be fairly described as disastrous. On the other hand, the figures of survival for treatment by closed methods are much more favourable.

No attempt has been made to separate cerebral from cerebellar abscesses, for the fundamental principles underlying closed methods are valid wherever the abscess is situated. Nor will etiology and bacteriology be discussed; cases have survived which exemplify all the recognized paths of infection, and once an abscess has developed the treatment of the primary focus is usually of secondary importance. Identification of the responsible micro-organism naturally demands appropriate chemo-therapy, but does not modify the surgical manœuvres. Sulphonamides were given in 15 cases, seven of which died; two of these had acute diffuse suppurative meningitis at autopsy. Chemo-therapy doubtless combats meningitis but it is questionable if it exerts any beneficial effect upon the abscess proper.

In order to determine, if possible, the reasons why treatment may fail, an analysis of the post-mortem findings has been made, and is instructive. An autopsy was performed in 16 of the 17 fatal cases. Extensive and massive œdema of the brain was observed in six cases (three drained, three aspirated); œdema to some degree is found around every brain abscess, but in these examples it involved a very wide area. In two of these cases pronounced brain herniation was noted. Diffuse leptomeningitis was present in five cases (four drained, one aspirated), and ventriculitis in three (all drained). Multiple abscesses were found in four cases—in three they were localized to one lobe, in the other they were scattered throughout the brain. Pulmonary embolism caused the death of one patient. Another died in status epilepticus whilst temporarily discharged from hospital awaiting final enucleation of the abscess which had been aspirated several times; the autopsy revealed a shrunken thick-walled abscess with no recent spread of the infection. Thus it would appear that treatment failed on account of multiple abscesses, massive œdema, or acute meningitis (including ventriculitis). Since the difficulties of successfully treating a solitary abscess are at present so great, it seems to me justifiable to concentrate one's attention upon them, and to leave out of consideration at present those presented by the case of multiple abscesses.

Of the etiology of brain œdema there is but little knowledge, and indeed there is no unanimity of opinion as to the pathological criteria of its lesser degrees, nor of its precise mechanism of development and spread. But when present in the severe degree to which reference has been made, its post-mortem recognition by the unaided vision is simple and unequivocal (Fig. 1*a*, *b*). Its

presence may be assumed clinically if there is marked drowsiness, lack of improvement as a result of treatment (in the absence of meningitis), and the neurological signs of brain herniation. Its treatment—in both abscess and tumour of the brain—constitutes perhaps the most urgent and the most formidable problem in neuro-surgery. Dehydration methods have had



(*a*)

(*b*)

Fig. 1(*a*).—Walled-off left frontal abscess, approximately 4 weeks " old," situated antero-lateral to tip of frontal horn of ventricle. Gross œdema, and cavitation of softened white matter. (*b*) Gross œdema of frontal lobe: cavitation, communicating with ventricle. No macroscopic communication with abscess cavity.

(Case not included in series; sudden death before treatment could be started; severe temporal lobe herniation.)

and are still having a great vogue. In my experience I must confess that all the methods of dehydration have proved disappointing. Occasionally there has been a transient diminution of drowsiness, but I can recall no case of suspected severe brain œdema in which enduring and indisputably curative effects have been obtained by energetic dehydration. Autopsy has revealed severe œdema in spite of such treatment. It is possible that in the lesser

degrees or in the early stages of brain œdema, dehydration therapy may control the process by diminishing a raised intracranial pressure and improving the cerebral circulation; but this remains to be proved. I have been frequently impressed how in some cases œdema persists and spreads in spite of treatment, in a manner best described as fulminating and malignant.

By reason of the observations at autopsy of the disturbances of the brain that œdema causes, and of the results of treatment, my opinion is hardening that the only hopeful line of attack is surgical decompression. This is by no means always successful, probably because it is not resorted to sufficiently early; and if advanced œdema is an irreversible change, this is almost certainly true. Decompression for brain abscess may be obtained by the Clovis Vincent procedure, and some measure of relief of tension results from the mere aspiration of the abscess. But the unopened dura mater beneath a bone flap will slowly give, and by reason of its greater degree of elasticity than the skull, affords an immediate though slight amount of relief to the brain and its blood vessels. Subtemporal decompression, and in cases of cerebellar abscess suboccipital decompression, are of similar value, and further details of the application of these methods will be given later.

The avoidance of meningitis and the treatment of the established condition vie with brain œdema in difficulty and importance. Chemo-therapy has helped, but other methods must be employed at the same time. Diffuse meningitis may occur at the same time as the spread of infection into the brain, or it may be due to the surgical activities. During drainage it is very liable to occur as a direct spread over the surface of the brain, and the two-stage method was introduced to cope with this. Infection may also spread centrifugally, probably as a result of the dislocation of the infected area towards the craniotomy and the consequent disruption of the delicate newly formed natural barriers to micro-organisms. Operative and autopsy studies show that at the deepest pole of an abscess its wall is thinnest, and it is from this area that secondary loculi commonly form. From this poorly walled-off pole of an abscess there is a most important potential pathway of infection to the subjacent ventricle; œdema softens the intervening white matter, and the ependyma of the underlying ventricles may rupture into this softened area. (Fig. 1*b*) Finally, as is well recognized, the ventricle tends to wander as a diverticulum through the softened white matter towards the brain fungus which may develop as a result of drainage, and the diverticulum can easily rupture on its surface. On several occasions, during the enucleation of an abscess its wall has been found adherent to that of the ventricle; treatment by drainage would almost certainly have led to ventricular infection, either by penetration by the drainage tube, or in methods relying on the extrusion of the abscess wall by rupture of the contiguous ventricle.

The accepted treatment of acute suppurative meningitis uncomplicated by abscess is to maintain the patency of the cerebrospinal fluid channels by frequent lumbar puncture and the free administration of fluids—" forced drainage "—and chemo-therapy. Of the latter no more will be said. If an abscess is present, the subarachnoid spaces are inevitably obstructed by the

swelling of the brain and by the herniation of brain into the various cisterns. Thus attempts to drain cerebrospinal fluid by lumbar puncture lose effectiveness, and indeed are dangerous by accentuating herniation. Thus some decompressive measure is as logical a form of treatment for the meningitis as for the œdema.

These experiences with various methods of treating brain abscess show how results led to the adoption of closed methods, and why these methods may be expected to give better results than drainage. The various procedures which are undertaken in a given case will now be outlined.

Successful treatment depends upon accurate diagnosis; this must include precise localization, an estimate as to the "age" of the abscess, and the presence or otherwise of meningitis. These matters cannot be discussed here except to state that so essential is early and accurate localization that no ancillary method should be ignored. A diagnostic burr-hole and tapping may be all that is necessary for confirmation in some cases; on the other hand, one should never hesitate to employ ventriculography. In the latter event—parallel with tumour surgery—an osteoplastic flap should be reflected forthwith, and the abscess contents evacuated through a wide-bore blunt needle. At what point in the course of the evolution of an abscess should operation be undertaken? While there is good clinical evidence that the patient is successfully resisting the infection and localizing the process which is in its early stages a suppurative encephalitis, surgical interference should be withheld. But when the clinical state is clearly deteriorating, or if the surgeon is in doubt, then it becomes necessary to aspirate with or without some type of decompression. In the second series of cases, aspiration was undertaken in the first week of the illness in two cases, the second week in nine, and in the remaining seven cases during the third, fourth, fifth, eighth, and twelfth weeks. When aspirating an abscess, the operation field should be swamped with a bactericide such as proflavine, to avoid its infection. It will often be found that with the emptying of the abscess, the dura mater becomes quite slack. If, however, tension is not sufficiently relieved, the dura mater should be opened so as to provide an orthodox osteoplastic subtemporal decompression. Even if the dura mater is not opened, bone should be removed from the base of the flap so as to provide a gradual decompression. A burr-hole is made in the bone flap over the most superficial part of the abscess through which it may be subsequently aspirated, as recommended by Clovis Vincent. When a diagnostic tap reveals an abscess conveniently accessible, or where there is but little swelling of the brain, decompression may not be needed. It may be postponed if the patient's condition is too grave to allow of it, or it may be needed at a later date if evidence of œdema accumulates. In cases of cerebellar abscess, provided the patient's condition allows of it, I think that the dura mater of the posterior fossa should be fully exposed in every case; the abscess can be aspirated more easily than through a burr-hole behind the mastoid process. But the dura mater should never be widely opened owing to the proximity of the cisterna magna, and the consequent ease with which diffuse meningitis can occur. The aspiration of a cerebellar abscess affords much

greater relief of tension than aspiration of a hemisphere abscess, owing to its strategical position in causing an obstructive hydrocephalus.

At the time of aspiration, the cavity of the abscess is irrigated with electrolytic sodium hypochlorite (Milton). Using small quantities (less than the amount of pus obtained), 50 per cent. Milton is allowed very gently to flow into the cavity and is then aspirated. This is repeated several times, and a large quantity of ropy pus can usually be obtained, which would otherwise be too viscid to pass through the needle. When the fluid returns fairly clear, it is valuable to leave in the abscess a small quantity of 5 per cent. Milton or of 1 in 1,000 buffered solution of proflavine. A bactericide in such a closed cavity appears to aid in the destruction of organisms (three abscesses have become sterile under treatment) and to accelerate the localization of infection and the maturation and contraction of the abscess. It is also a prophylactic against infection of the needle track. At first it may be necessary to repeat aspiration every few days, but the intervals will gradually lengthen. The patient's condition, the amounts of pus obtained, and the resistance of the abscess wall are all factors which should be weighed in making a decision to re-aspirate. In temporal or cerebellar abscess the aspirating needle must be inserted through layers of muscle, and to facilitate this it may be wise on each occasion to reopen the small wound made for " tapping " purposes so as to expose the dura mater and under direct vision to make a small nick in it, through which the needle is passed. Elsewhere, a small incision through scalp and dura mater made with the point of a tenotome is all that is necessary; in each case the skin (and muscles) are completely closed again by sutures at the end of the aspiration. These precautions are taken to avoid any force being communicated to the cranial contents, and to prevent sinus formation and secondary infection.

Thorotrast (1–2 c.c.) injected into the abscess at one of the early aspirations is of great help. It gradually becomes " fixed " in the wall of the abscess and the size and the position of the abscess can be demonstrated radiologically. One might expect that the need for re-aspiration would be indicated by an increase in the size of the opacity. However, such helpful information has rarely been obtained, and this suggests that deterioration in the patient's condition is more frequently due to increase of œdema (or spread of infection) than to increase in the quantity of pus. But much aid of a different character is obtained. In the course of time, the thorotrast opacity diminishes in size and gains in crispness of outline, assuming a somewhat crenated appearance, pari passu with the organization of a well-formed abscess wall (Fig. 2). Thorotrast may fail to depict the whole of an abscess if there are several loculi. This happened in one case (Fig. 3*a*, *b*); over confidence in the X-ray appearance led me to forget the possible presence of a deeper loculus, which was thus inadvertently ruptured and the patient died of a diffuse meningitis.

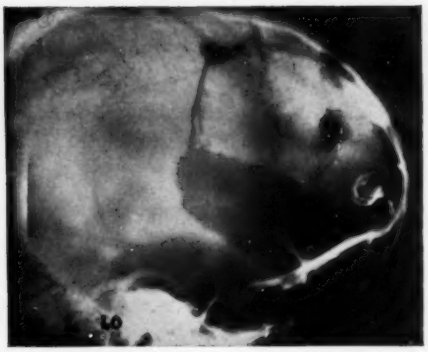
What criteria guide one as to when to enucleate the abscess? The pathological desiderata are the subsidence of all acute inflammation and the formation of a tough wall. This will correspond with the disappearance of toxæmia and of meningitis, diminution of symptoms of raised intracranial pressure—

and a softening of the decompression—and diminution in the neurological signs of a focal cerebral lesion. These signs may in fact disappear or they may become a crisp and stable residuum. The toughness of the abscess wall can be estimated by the blunt aspirating needle, and by the radiological appearance of the thorotrast shadow. I consider that there is a well-defined optimum period for successful enucleation. The above pathological criteria

13.2.40.

22.2.40.

7.3.40.



17.4.40.

Fig. 2.—Thorotrast visualization of abscess cavity and of abscess wall.

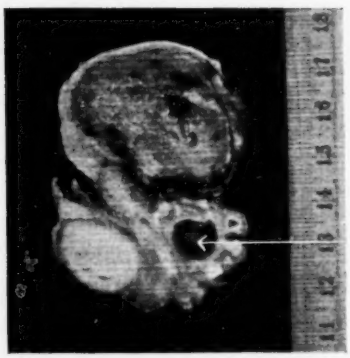
must be satisfied for obvious reasons. But if operation is unduly postponed, it becomes technically more difficult owing to the formation of an excessive degree of scarring around the abscess; firm trabeculæ may radiate from the abscess, leading to an unnecessarily wide excision of tissue. Secondary loculi or separate deeply placed abscesses may develop if a case is left too long. In contrast, during the optimum period, the abscess wall is well defined, is sufficiently tough to handle, and separates cleanly from the surrounding white matter. In this series, the age of the " youngest " abscess has been six weeks, and of the " oldest " six months, estimating age from the first symptoms of intracranial disorder. I judge that the third month (i.e. between 8 and 12 weeks) is usually the " time of election " for enucleation.

Enucleation is facilitated by uncapping the wall of the abscess excising with that portion of brain the adherent area of dura mater, which constitutes

the scarred track of the aspirating needle. When dissecting around the abscess, one must be ever alert for any prolongation of the abscess in a totally unexpected direction. The deeper the dissection the greater the care to be exercised to avoid rupturing its wall. If the abscess is large and tense it is

(*a*)

Thorotrast.



(*b*)

Thorotrast filled loculus.

Fig. 3 (*a*).—Radiograph of specimen: thorotrast in one loculus of abscess. (*b*) Specimen: thorotrast in only one of three loculi: the largest and thin-walled was deepest in the brain.

helpful partially to aspirate its contents, taking precautions against contaminating the field and the instruments, and the small hole must be closed by sutures. When the abscess is adherent to the wall of the ventricle, an opening into the latter may be unavoidable. In cerebellar abscess, the dis-

section is more difficult owing to the proximity of cranial nerves, and the abscess may be adherent to the dura mater covering the posterior surface of the petrous bone.

It is well recognized that epilepsy may follow the healing of an abscess, and enucleation may very likely avoid or diminish the frequency of this unfortunate sequela. But until the abscess has been finally eradicated an anti-convulsant should be given. In two of the present cases, fatal status epilepticus occurred after the patient left hospital. In one case the abscess had been drained, and had healed completely; the other has already been referred to. In neither case did an autopsy reveal any recent exacerbation of infection.

It is clear that closed methods of treating a brain abscess necessitate primary union of all incisions. Consequently, a brain abscess which develops underneath an open wound such as might result from an infected compound fracture of the skull, may have to be treated by drainage; and a small superficial abscess (which could be considered as virtually subdural in position) might possibly be more suitably treated by drainage. But these are the only cases in which I should now discard methods of non-drainage, although each must be considered upon its own merits.

If the results of treatment by open and closed methods are examined again, it will be seen that they really reflect the morbidity of the disease at different stages in the course of treatment. Some die in the early stages, and extensive œdema was present at autopsy in all three cases which died following aspiration; the fatal issue might have been prevented by decompression, but there is no good reason to suppose that drainage would have been more successful. Of the five that died after aspiration and decompression, in only two was there extensive œdema. Only one case died out of seven in which enucleation was carried out, and this roughly indicates the relatively low risk of a fatal issue provided the early dangers can be safely overcome.

AN EXPERIMENTAL APPROACH TO THE DETERMINATION OF COMPARATIVE EFFICIENCY OF INSULIN AND CONVULSION THERAPY

BY

H. A. PALMER, Major, R.A.M.C.

(RECEIVED 23RD FEBRUARY, 1942)

THE literature of hypoglycæmic and convulsant therapies has now reached imposing proportions. It would appear that whereas insulin therapy is finding more statistical justification in treating "Dementia Præcox," convulsant therapy, especially now that we have curare available, is establishing a special claim for consideration in the affective disorders of the later age groups.

The question of their comparative utility in the hands of the same investigator is still a justifiable field for research. My experience with cardiazol is of much longer duration than my experience with insulin, while my experience with electrically induced convulsions is necessarily short.

The case material of this research comprehends the intake of a military mental hospital and differs considerably from that of the civilian English mental hospital. It approximates to that of the Woodside or Maudsley material in this country and the Phipps, Philadelphia, and two larger New York clinics in the U.S.A.

Such military material has the advantage of dealing with relatively healthy male adults within the age periods 20 to 50, and in general covers a prognostically favourable group of patients.

A large proportion of the patients were sad, and ill on account of their sadness, but viewed as clinical syndromes, they showed schizophrenia characterized by autistic modes of thought and the frequent occurrence of bewilderment. Finally, it may be said that there was underlying hysteria in nearly all the cases, in the sense that the illness had meaning, though subconscious, for the personality.

Military material does not lend itself to orthodox classification and any attempt to do so results in therapeutic wastage.

The method of selection for inclusion in the experiment was as follows : If a patient was admitted whose prognosis did not seem immediately favourable or, as in the case of the more completely syntonic syndromes, who had not responded to a regime of narcosis therapy; or if the patient's conduct or clinical characteristics had serious effect on his immediate well-being, future progress or ward atmosphere, that patient was in most instances subjected to a course of insulin or convulsant therapy. On 10th January, 1941, 7 per cent. of patients in hospital were receiving insulin therapy and 13 per cent. were

receiving convulsant therapy, making a total of 20 per cent. on shock therapy; and 5 per cent. were on narcosis therapy.

The method of allocation to either of the two therapies was as follows: Every alternate case was given insulin or cardiazol, for 40 consecutive cases. The next 10 cases in order were given cardiazol, the following 10 cases insulin, and the final 30 cases were given electrical convulsions. A small group of 10 controls intervened between the first 60 cases and the final 30 cases. This control part of the experiment had to be discontinued; it threatened a choking of the clinic's turnover, which in war-time is an important consideration, and produced an unfavourable effect on ward atmosphere and the efficiency of the personnel.

The sole purpose of the enquiry was to effect a comparison between the individual therapies. Permanence was outside its scope. The convulsant regime was continued until the patient was symptom free, and was usually given three times a week on alternate days. The mean number of convulsions given was 10 per patient.

The insulin regime was given over a period of a month and on the average included 20 comas whose duration lasted an hour. The depth of coma produced can only be stated in terms of the fact that it reached the limit of safety in most cases. In 571 comas, 18 fits, 10 prolonged and two irreversible comas occurred.

The table on p. 12 sets out the results achieved:

Each patient was allotted a score. Ten marks were given for apparent recovery to full economic efficiency and full remission of symptoms. The total possible score was therefore 300 in each group.

The results of this experiment may be stated as follows: The convulsant and insulin technique produced approximately equal numbers of remissions and cures, but the convulsant group showed a small superiority. This finding was confirmed by the superior yield of recoveries following a second alternate therapy in which previously unsuccessfully treated cases are submitted to the other forms of therapy. The results with convulsant therapy are achieved more rapidly, more economically as regards apparatus and drugs, staff time, and period of in-patient treatment. No clear deductions appear justifiable concerning the type of case which might appear to do better under one as opposed to the other therapy. The impression was formed that a previous regime of narcotization gave a better outlook for subsequent therapy by either method—possibly especially the convulsant methods. The graduation made possible by insulin, though it was assumed to render such therapy susceptible of application to certain patients whose cardio-vascular apparatus might contra-indicate convulsant therapy, is partially countered by the cases in which collapse on small doses of insulin was followed by successfully carried out convulsant regime.

The most interesting clinical observation was the frequency with which convulsant treated patients in the course of their treatment would quite suddenly shift the topic of their preoccupation, as they commenced to improve. Thus, a hypochrondriacal man, previously preoccupied with his abdomen,

Table of Results

NO. OF CASES	THERAPY	MAINLY SYNTONIC SYNDROMES	MAINLY SCHIZOID SYNDROMES	SCORE	TOTALLY REFRACTORY TO 1ST REGIME	SUBSEQUENTLY CONSIDERABLY IMPROVED TO 2ND REGIME	TOTAL CONVUL-SIONS	AVERAGE	TOTAL COMAS	AVERAGE
30	Cardiazol	5	25	268	0	0	245	8	—	—
30	Insulin	4	26	238	5	4	—	—	571	19
30	Electricity	6	24	247	5	4	318	10	—	—
10	Control	2	8	31	6	6	—	—	—	—
6	Refractory as controls, subsequently treated	1	5	86	0	—	—	—	—	—
	Totally refractory to all therapy	0	1	0	—	—	—	—	—	—

It should be noted that of the total of 100 cases, all save one patient were discharged to their homes. Of these 100 cases, 75 per cent. were subsequently examined by an independent Medical Board for purposes unconnected with this research and found to possess less than 20 per cent. disability for civilian employment ; only 5 per cent. were considered unfit for civilian employment. The average stay in hospital was 2½ months.

began to discuss his wife's infidelity; a hitherto confused man began to discuss homosexual practices, and finally ceased to be concerned about these in turn; a clerk, previously exhibiting obsessional modes of thought revolving around past sexual misdemeanours, began to discuss his disappointment concerning promotion in the Army.

This sudden shift was not characteristic in the insulin group who exhibited more archaic content in the post-comatose phase.

In this clinic consequent upon the above findings insulin is only given to cases proved refractory to convulsant therapy and cases with poor physique. Approximately one patient receives insulin for every five receiving convulsions.

There remains the problem of spinal fractures complicating convulsant treatment, which in my experience continues to be met with in not less than 15 per cent. of cases. In July 1939 I first advocated (Palmer, 1939) and used curare as a means of controlling this complication. This work was apparently entirely successful and was carried out with the help of Dr. Keale in the psychiatric department of Dr. Noel Harris at the Middlesex Hospital. The outbreak of war put a temporary stop to this work which was inspired by Ranyard West's work in 1936 in this country on tetanus. Meanwhile, in a less disturbed clinical atmosphere in U.S.A., similar work was published (Bennett, 1940), with the result that a marketable product has become available.

Summary

A method of comparing insulin and convulsion therapy in mixed military cases under otherwise standard conditions was applied to 100 patients selected from amongst 637 admissions to a military hospital. The results show a very nearly equal efficiency for the two methods, but with the convulsant methods slightly more efficient, very much cheaper, and easier to apply. Occasional cases reacted well to one form of therapy, having previously shown no reaction to the other. Electrically induced convulsions produced results as efficiently as peptazol induced convulsions. There is slight evidence that cardiazol produces better results than electricity.

To Captains Tredgold, Graham, and Smith I am indebted for the fullest co-operation in enabling the research to be carried through over a prolonged period.

REFERENCES

Bennett, A. E. (1940). *J. Amer. med. Ass.*, **114**, 322.
Palmer, H. A. (1939). *Lancet*. **2**, 181.
West, R. Ranyard (1936). *Lancet*, **1**, 12.

THE ACTION OF ADRENALIN IN NEUROTICS

BY

A. S. THORLEY

From an E.M.S. Neurological Unit.

(RECEIVED 26TH FEBRUARY, 1942)

Literature

SINCE Cannon (1915) demonstrated that emotional stress is associated with an increased and prolonged secretion of adrenalin, attention has been directed to the relationship of the effects of adrenalin and the symptoms of anxiety. Maranon (1924), giving subcutaneous injections of the drug, observed effects varying from a vague apprehension to severe emotional disturbance and concluded that an exaggerated response is shown by anxiety neurotics. He demonstrated that emotion is not directly determined by the physical phenomena and that intense physical reaction can occur without emotional response. The emotion may not necessarily be that of fear, and a case experiencing great joy was described.

Richter (1940) suggested that the emotional response may be due to the physical effects of the injection and claimed to have eliminated this by the introduction of adrenalin electrically through the skin. By this method he confirmed Maranon's findings, agreed that emotions other than fear may occur, and described an asthmatic who experienced a sensation of confidence after injection. He concluded that conæsthetic impulses arising from visceral disturbances excite an emotionally charged cortical pattern so that each tends to increase the degree of excitation of the other.

Lindemann and Finesinger (1938) injected mecholyl and adrenalin intramuscularly into a group of neurotics. They objected to the intravenous route on the grounds of the rapid rise and fall of blood pressure which occurs and preferred the slower intramuscular route as it gave time for more prolonged observation. They found four groups: (1) specific response to adrenalin, (2) specific response to mecholyl, (3) reaction to both drugs, (4) no response to either. In the adrenalin-sensitive group the anxiety attacks were found to be unrelated to specific situations or mental content and were thought to coincide with Freud's " actual neurosis." The mecholyl-sensitive group were those with definite phobias and fears. The mixed group had a history of autonomic instability and hypochondriasis and the last group indicated more profound personality disorders. The writers recorded that in the adrenalin attack there is a surrender to anxiety, associated with diminished speech production, while in the mecholyl attack there is an active attitude directed to the environment, with increased speech production, associated with phobic states.

To return to the physiological aspect: the question arises as to what constitutes a normal response in terms of rise in blood pressure and pulse rate to the action of adrenalin. Clark (1940) states that in response to 1 c.c. adrenalin injected subcutaneously, the blood pressure may rise 75 mm. Hg in the sympathicotonic, 20 mm. in the normal, and may fall 10 mm. to rise 10 mm. in the vagotonic individual. It is impracticable to discuss adequately here the literature concerning this classification. Kuntz (1934), reviewing the wealth of papers which has accumulated since Eppinger and Hess (1909) postulated vagotonic and sympathicotonic types, quotes Petsen and Thorling's criticisms, chief of which are that symptom-complexes of vagotonia, e.g. asthma, may have sympathetic symptoms and may over-react to sympathetic stimuli, and similar observations can be made about sympathicotonia, e.g. hyperthyroidism.

Misch (1935), in discussing the genesis of the syndrome of neurotic anxiety, considers the acute major attack to be a sympathetic phenomenon followed by a para-sympathetic swing, and in the chronic form to exhibit a mixture of sympathetic and para-sympathetic symptoms. In addition, he refers to Oppenheim (1909) as having postulated a congenital weakness of the vasomotor visceral apparatus and saying that anxiety has not only a somatic but also a psychical origin, resting on an unusual reaction of the vegetative nervous system to ideas and sense impressions. Evidence of this neuro-circulatory inadequacy has been shown by McFarland and Huddleson (1936) by use of the Schneider Index (an index of the changes in pulse rate and blood pressure when the patient changes from lying to standing and has an undue response to an exercise tolerance test). The index is markedly raised in anxiety states as compared with other forms of psychopathy and with normal individuals.

On this evidence it remains open whether, in cases of anxiety neurosis, (1) sensitivity is expressed as an over-reaction physiologically to the drug, (2) sensitivity is an over-reaction mentally to visceral sensations that are no more marked than in the normal individual, or (3) both mechanisms are playing a part.

Clinical Material

Thirty-five patients, comprising three main groups, (1) anxious, (2) anxiety +other features, (3) not anxious, were investigated. The first described the visceral sensations accompanying fear in a severe form and arising from experiences in the Battle of France, air-raids over this country, or the rigours of service life. It appeared that their physiological equilibrium was unduly unstable and that they were upset by stimuli that did not have such a severe effect on the majority of their comrades. They were usually of the asthenic physique and showed such indications of instability as a tendency to be easily intimidated, worry over trifles, flush easily, and lack self-confidence.

The second group, in addition to anxiety, present other important features, such as hysterical amnesia, depression, or symptoms referable to a head injury of some severity. The last group was a miscellaneous collection not obviously

presenting somatic anxiety and consisted of patients suffering from gastric neuroses, stammer, and organic syndromes.

Of the fifteen patients in the anxious group, the symptoms of twelve had been aggravated by enemy action and of the other three by the conditions of service life. In six of these patients a near relative had shown definite evidence of mental disorder. Thirteen showed previous evidence of neurotic traits and all exhibited some such personality defect as shyness, timidity, excessive worrying, and undue sensitivity.

Of the eleven patients in the second mixed group, the symptoms of seven had been precipitated by bombing and of the remainder by service life. Eight had evidence of familial psychopathy, eight showed previous neurotic traits, and in all there was a defect of personality.

In the third group of nine non-anxious subjects, four had a positive family history of mental instability, five had previous neurotic traits, and seven had minor personality defects.

Experimental Method

The effects upon the pulse and blood pressure and the symptoms noticed by each patient after an intramuscular injection of adrenalin have been recorded. The intramuscular route was chosen because of the violent symptoms produced by the intravenous method.

Before the administration of adrenalin, saline was given intramuscularly, to accustom the patient to an injection, and was repeated if there was an undue response. In spite of the saline injections, it was impossible to prevent the subjects realizing that a drug had been given, and they complained of the local pain produced. Before an estimate of the effect produced by adrenalin could reasonably be made, it was essential to obtain a fairly stable pulse rate and blood pressure. This proved unexpectedly difficult, and in one particularly apprehensive subject, his nervousness, tremor (which was increased by the tightening of the sphygmomanometer band), palpitations, and præcordial pain disappeared only after 50 minutes; during this time his systolic blood pressure fell 35 mm. Hg. The difficulty generally experienced, however, was in waiting for a diminution in the range of oscillations rather than in a steady fall of the readings. In one patient, after saline the systolic blood pressure oscillated from 150 to 115 mm. Another patient fainted while his blood pressure fell to 80 mm. and his pulse to 60 per minute after an injection of saline. The systolic blood pressure was considered to be " resting " when it did not vary more than 10 mm. during a period of 5 minutes before injection. The highest pulse rate or blood pressure reading reached after injection, less the highest figure in the " resting " period, constituted the presumed response to adrenalin. The readings were continued until the blood pressure was obviously going to fall consistently—a period lasting up to half an hour.

In order to reassure patients, they were examined while sitting comfortably in a chair. Two series of adrenalin doses were given: amounts of the order of 1 c.c., to make a comparison with Clark's figures, and smaller quantities

because it was thought that with such an amount undue sensitivity would be more apparent.

Results

None of my patients, in response to adrenalin, produced effects outside the limits given by Clark's Pharmacology, as quoted above. In the following observations a rise in blood pressure greater than 20 mm. Hg is considered to be a brisk response. If it is justifiable to take Clark's figure of 20 mm. as a normal response to 1 c.c. adrenalin injected intramuscularly, it is certainly reasonable with smaller quantities. Since no similar arbitrary figure for pulse rate has been encountered in the literature and as only two patients in the whole series gave a rise in pulse rate greater than 30 beats per minute, this factor does not warrant further consideration.

In view of possible criticism of the findings obtained from sitting patients, eight subjects were examined lying down (Table II). Of nine sitting patients, five showed a significant rise in blood pressure, and of the eight lying patients, the blood pressure rose markedly in three. Although the number is small, there is nothing in the findings to suggest that posture affects the changes in blood pressure resulting from intramuscular injections of adrenalin.

As already mentioned, patients were divided according to dose into two groups: small (0·5 to 0·75 c.c.) and large (0·8 to 1·2 c.c.). Table I shows that eight out of twenty-four patients had a rise in systolic blood pressure greater than 20 mm. Hg, as had eight out of sixteen subjects receiving the larger dose (Table II). One expects such a finding, but a glance at the tables shows that the extent of rise in blood pressure is not proportionate to the dose of adrenalin. The seven cases marked by asterisks in Tables I and II are common to both groups. Of the four patients whose blood pressure did not rise significantly in response to a small dose of adrenalin, only one gave an undue rise of blood pressure with the larger dose. Although there is a tendency for larger intramuscular injections of adrenalin to produce greater rises in blood pressure, the rise is by no means directly proportionate to the dose.

As far as the question of whether anxious patients show an undue rise of blood pressure is concerned, of those receiving a small dose, five out of eleven in Group I, one out of six in Group II, and two out of seven in Group III gave significant responses (Table I). In the larger dose-group (Table II), the comparable figures were: Group I, four out of seven; Group II, three out of seven; Group III, one out of three. Using the small dose, a greater number of patients of the anxious class appear to be unduly sensitive, but the figures are too small to meet statistical requirements.

It may be thought that the differences between the effects of the various injections of adrenalin are due to variations in the rate of absorption. The following observations indicate that other factors play a very important part in determining any individual response. Case I (1) in Table III, whose systolic blood pressure fell in response to an injection of saline, after experience of adrenalin responded by a rise in blood pressure to saline; thus indicating a

TABLE I.—SMALL DOSE (0·5 TO 0·75 C.C. ADRENALIN) †

CASE NO.	DOSE	RISE B.P.	RISE P.R.
I (1)*	0·5	40	8
(2)*	0·5	10	20
(3)*	0·5	30	30
(4)	0·5	20	8
(5)	0·6	25	12
(6)	0·6	25	8
(7)	0·6	15	16
(8)	0·6	15	−8
(9)	0·65	20	4
(10)	0·7	20	4
(11)	0·75	25	24
II (1)* (*a*)	0·5	−10 to +10	−8 to +8
(*b*)	0·6	25	4
(2)*	0·5	10	8
(3)*	0·6	15	16
(4)	0·65	20	4
(5)	0·7	10	8
(6)	0·7	15	0
III (1)*	0·5	15	4
(2)	0·6	10	20
(3)	0·65	5	8
(4)	0·65	15	4
(5)	0·7	20	4
(6)	0·7	35	12
(7)	0·75	25	24

TABLE II.—LARGE DOSE (0·8 TO 1·2 C.C. ADRENALIN) ‡

CASE NO.	DOSE	RISE B.P.	RISE P.R.
SITTING			
I (1)*	0·8	40	4
(2)*	1·0	5	−4
(3)*	1·0	45	−8
II (1)	0·9	15	24
(2)*	1·0	30	12
(3)*	1·0	15	4
(4)	1·0	35	20
(5)*	1·2	35	12
III (1)*	1·0	20	4
(2)	1·0	15	20
LYING			
I (1)	0·8	20	12
(2)	0·85	20	36
(3)	0·9	25	12
(4)	0·9	25	12
II (1)	0·85	20	16
(2)	1·0	20	20
(3)	1·0	20	16
III (1)	0·9	30	20

* Cases common to both groups.
† Dose estimated on basis of 0·1 c.c. adrenalin per kilogram body weight.
‡ Dose estimated on basis of 0·1 c.c. adrenalin per 0·2 sq. metres surface area.

TABLE III

CASE NO.	EXPT.	RESTING PERIOD	DRUG	RISE B.P.	RISE P.R.
I (1)	(*a*)	10 mins.	Saline.	−10	4
		10 ,,	0·6 c.c. adrenalin.	20	4
	(*a*)	23 ,,	Saline.	25	−8
	(*b*)	28 ,,	,,	15	0
I (2)	(*a*)	14 ,,	0·6 c.c. adrenalin.	25	20
	(*b*)	38 ,,	0·6 c.c. ,,	40	16
	(*c*)	36 ,,	0·6 c.c. ,,	55	32
	(*d*)	55 ,,	0·1 mg. acetyl-choline.	−10	−6
	(*e*)	34 ,,	0·1 mg. ,,	+5	0
		25 ,,	0·6 c.c. adrenalin.	20	−4
	(*f*)	42 ,,	0·6 c.c. ,,	35	4
I (3)	(*a*)	43 ,,	Saline.	−5	0
		11 ,,	,,	10	12
	(*b*)	11 ,,	,,	−20	4
		43 ,,	,,	10	8
	(*c*)	40 ,,	0·1 mg. acetyl-choline.	−5	16
	(*d*)	42 ,,	0·5 c.c. adrenalin.	20	8
	(*e*)	59 ,,	Unexpected pistol shot.	15	0
		11 ,,	,, ,, ,,	20 to −10	8
		8 ,,	,, ,, ,,	0	0
		6 ,,	0·5 c.c. adrenalin.	−10	0
		8 ,,	Unexpected pistol shot.	0	0
		4 ,,	,, ,, ,,	−15 to +15 to −20	4 to −4
II (1)	(*a*)	40 ,,	0·6 c.c. adrenalin.	5	−4
		22 ,,	0·1 mg. acetyl-choline.	−10	4
		23 ,,	Psychological stimulus.	35	24

factor of " expectancy." Case I (2) in the same table illustrates the effect of increasing apprehension of the test and a fear of the visceral sensations produced. The blood pressure and " resting-time " increased with each successive experiment; the responses to saline have been omitted as no striking features were shown. This " conditioning " effect was temporarily removed by substituting acetyl-choline (also painful) for adrenalin, although the subject was able to detect the difference between the subjective effects of the two drugs. The findings suggest an increasing response to the visceral sensations produced rather than a reaction to a local painful injection. Case I (3) illustrates that a subject's systolic blood pressure may fall further in response to saline than to acetyl-choline, though his response to adrenalin remains normal; when frightened by the unexpected firing of a pistol, his blood pressure fell in response to adrenalin but subsequently oscillated violently when another shot was fired. On another occasion, this subject's blood pressure rose 45 mm. and his pulse rate 24 at reference to such painful topics as knives, suicide, and Southampton air raids, and also on serially subtracting seven from 100. Case II (1), who had shown a normal response to a small dose and a brisk response to a larger dose of adrenalin, was practically unmoved by 0·6 c.c. adrenalin after his discharge from the Army. A reference to this topic, however, 45 minutes later, and in spite of an intermediate injection of acetyl-choline, gave a rise in blood pressure of 35 mm. Hg and an increase of 24 beats a minute in pulse rate.

Such results as these show the impracticability of the concepts " sympathicotonia " and " vagotonia." They illustrate the importance of emotional factors and previous experience of the drug in determining blood pressure responses.

Subjective Findings

Table IV gives the frequency with which various symptoms and signs occurred in each clinical group, under the varying conditions of the onset of experimental situations, receiving injections of saline and adrenalin. As the results vary when the test is repeated, only the responses to the first experiments and injections of saline and adrenalin respectively are given. Since patients were encouraged to give their descriptions spontaneously, accounts depend on the form of neurosis, intelligence, and co-operation of the subject. Such physical signs as tremor, changes of colour, holding the breath, and sweating (central, i.e. sweating of palms) have been included only if they were obvious or were complained of by the patient. In order to discover whether any correlation exists between symptoms and rise in blood pressure, the patients have been divided into two groups: those in whom the systolic blood pressure rose more than 20 mm. Hg and those who did not exhibit such a change. The incidence of symptoms was greater in the anxious subjects in response to the situation, saline, and especially adrenalin in the group which did not show a significant rise of blood pressure.

It is of interest to note that one patient burst into tears after the injection

of adrenalin because the resultant sensations, tremor, and " stomach turning over " reminded him of an occasion when his Commanding Officer accused him of malingering. One patient distinguished between the symptoms produced and those of an anxiety attack by mentioning the absence of the " hot feeling," and another made the distinction by the absence of the " sinking sensation in the stomach." This latter described the sensations after an injection of acetyl-choline followed by adrenalin as " like an attack—he had a sensation of fear which he was holding in." In five of the lying patients, fifteen minutes after adrenalin, when they had passed their maximum response, further symptoms were brought out by asking the patient to stand up, and in four of them an Exercise Tolerance Test increased the symptoms present or produced further ones. No persistent effect was observed upon blood pressure. Symptoms so resulting were not included in the above tables.

TABLE IV

	GROUP I (8 PATIENTS)			GROUP II (9 PATIENTS)			GROUP III (6 PATIENTS)		
	SITN.	SAL.	ADREN.	SITN.	SAL.	ADREN.	SITN.	SAL.	ADREN.
Rise of Systolic B.P. less than 20 mm. Hg:									
Total No. symptoms ..	19	13	34	20	9	22	7	5	16
Average No. per patient	2·4	1·6	4·2	2·2	1·0	2·4	0·8	0·8	2·7
Rise of Systolic B.P. more than 20 mm. Hg:									
Total No. Symptoms	15	4	26	9	2	11	9	7	16
Average No. per patient	2·1	0·5	3·7	4·5	1·0	5·5	3·0	2·3	5·3

Nine patients had an unusually low blood pressure which oscillated around a figure between 90 and 110 mm. Hg. Seven of them had pure anxiety states in Group I and in three of these adrenalin produced a significant rise of blood pressure. The other two were in Group II and one exhibited an undue lability of blood pressure in response to a large dose of adrenalin.

These findings indicate that anxiety neurotics show a sensitivity to intramuscular injections of adrenalin which is expressed in an increased number of symptoms referable to all physiological systems. Other factors, common in anxiety neurotics, not directly related to each other or to symptomatology, are the undue lability of blood pressure and an unusually low resting blood pressure. Such findings may occur in any psychoneurotic individual but occur more frequently in the constitutionally anxious types.

Summary and Conclusions

1. In a review of the literature the views of various authors upon the sensitivity of patients with anxiety state to adrenalin have been given. The observed sensitivity to adrenalin is generally regarded as being a common feature of anxiety neurosis.

2. Thirty-five neurotic service patients, forming three clinical sub-groups, were investigated. Evidence of familial psychopathy, previous neurotic traits, and inadequacies of personality were a marked feature in their previous records.

3. The difficulty of obtaining "resting" pulse rate and blood pressure readings and of deciding what constitutes an abnormal response is demonstrated.

4. With small intramuscular doses of adrenalin, a significant rise of blood pressure was found more frequently in patients with anxiety states than in those of other clinical sub-groups. The response varied from patient to patient and from time to time in the same subject. It did not vary proportionately with the dose of adrenalin and depended rather on the mental state of the patient, his previous experience of the drug, and his reaction to the visceral sensations produced.

5. In the absence of a rise in blood pressure, the appearance of symptoms is more frequent after adrenalin injections in anxiety states than in other groups. Sensitivity in subjective experience is not related to the labile blood pressure and the low blood pressure which are common features of this clinical group.

Acknowledgments

My thanks are due to Dr. L. Minski, Medical Superintendent of the Emergency Hospital, for permission to use the clinical material, and to Dr. Eliot Slater, Clinical Director, without whose kindly advice this work would not have been completed.

References

Cannon, W. B. (1915). Bodily Changes in Pain, Hunger, Fear and Rage. New York, 1st edition.
Clark, A. J. (1940). *Applied Pharmacology*. 7th edition.
Eppinger, H., and Hess, W. R. (1909) quoted by Kuntz (1934).
Kuntz, A. (1934). *Autonomic Nervous System*. Baillière, Tindall and Cox, London. 2nd edition.
Lindemann, E., and Finesinger, J. E. (1938). *Amer. J. Psychiat.*, **95**, 353.
Maranon, G. (1924). *Rev. franç Endocrin.*, **2**, 301.
McFarland, R. A., and Huddleson, J. H. (1936). *Amer. J. Psychiat.*, **93**, 567.
Misch, W. (1935). *J. ment. Sci.*, **81**, 389.
Oppenheim (1909) quoted by Misch (1935). *Berlin klin. Wschr.*, 1293.
Richter, D. (1940). *Proc. roy. Soc. Med.*, **33**, 615.

LISSAUER'S DEMENTIA PARALYTICA

CONTRIBUTION TO THE STUDY OF ITS DIAGNOSIS AND PATHOGENESIS

BY

A. J. GALBRAITH and A. MEYER

From the Central Pathological Laboratory, L.C.C. Mental Health Services.

(RECEIVED 16TH MARCH, 1942)

Introduction

CASES of general paralysis of the insane in which " focal " symptoms are a prominent feature, and which show circumscribed atrophy of parts of one or both cerebral hemispheres, have been grouped under the heading of Lissauer's Dementia Paralytica. Lissauer and Storch published their paper in 1901, but in Alzheimer's (1904) famous monograph there is mention of a number of cases of this condition which had been recorded prior to this. Since then further cases have been described. In 1932 Merritt and Springlova reviewed 35 cases previously published in the literature, and added eight cases which they had personally studied. In 1936 Ogino reported on three cases, and a year later Malamud's (1937) paper contained a description of four further cases. The latest studies on this subject by Dalke (1938) and Divry (1940) are unfortunately not available for comment in this paper.

The definition of the clinical syndrome and the description of the pathological findings, in cases of Lissauer's Dementia Paralytica, given by Merritt and Springlova, represents the generally accepted view on the condition up to the present time. These authors came to the conclusion " that Lissauer's Dementia Paralytica should be suspected in every case of general paralysis with apoplectiform or unilateral convulsions, especially when these are followed by localizing signs, e.g. hemiplegia, aphasia, hemianopia, etc."

The cardinal pathological feature, as previously indicated, is the presence of one or more areas of macroscopically apparent local atrophy, which are, with few exceptions, e.g. cases of Buder (1903) and Bielschowsky (1920) situated in the so-called " posterior " parts of the cortex. Indeed Alzheimer had already referred to the Lissauer type as general paralysis of the posterior cerebral cortex. Merritt and Springlova, and later Ogino, have regarded the distribution of the atrophic areas in most cases as being intimately related to that of the middle cerebral artery. The histological picture in the regions of the cortex which are not markedly atrophic is one of the usual G.P.I. process, often comparatively mild. On the other hand, the areas of local atrophy

present features which differ considerably from those seen in the non-atrophic regions. The most prominent, and according to Malamud the essential change found in the atrophic areas is status spongiosus, first described by Fischer in 1911. This is characterized by extensive loss of all the component parts of the parenchyma, with an imperfect replacement by glial tissue. The end result is the formation of a coarse glial reticulum, lacking in both " ground substance " and cellular elements. It is frequently laminar, involving especially layers II and III. In the white matter of the atrophic areas a somewhat analogous state of affairs may be present. Thus demyelinization followed by gliosis frequently results in a typical status spongiosus. Evidence of an inflammatory reaction is usually less than in the non-atrophic regions, and the iron reaction (" Paralyseeisen ") is characteristically weak or may even be negative.

The problem of pathogenesis in Lissauer's Dementia Paralytica has been widely discussed since the original publication of Lissauer and Storch, and various theories have been proposed. The trend in recent years has been to introduce a vasomotor factor (Merritt and Springlova), or to explain the pathological changes in terms of colloid chemistry (von Braunmühl, 1932, 1933). Since our own case seems to be of special interest with regard to pathogenesis, it will be described first, and its significance in relation to the pathogenetic problem will be discussed later.

Clinical History

Mrs. D. B. Aged 40.

Family History.—Negative for mental disorder.

Personal History.—The patient was stated to be obstinate and subject to " tantrums " during childhood. Before her marriage she was employed as a dressmaker. She took no serious interest in the opposite sex until she met her future husband whom she married in 1924, when she was 27 years old. There are four children by this marriage. During her adult life she was described as being of a " cheerful and affectionate nature, but inclined to be irritable and obstinate." She had apparently no special interests beyond her home and had few friends.

No history of alcoholism.

Scarlet fever when æt. 34.

History of Present Illness

The patient's husband was killed in an accident in 1931 (Pt. æt. 34). Following the death of her husband she seemed to lose interest in everything and became neglectful of her person and her children. In 1934 she became subject to fits of excitement during which she would throw things at anyone who happened to be near at hand. She was eventually removed from home and admitted to Bexley Hospital on 5/7/34. At this time she was described as being garrulous and excitable. She recounted how for several weeks previously she had felt confused and had " terrible feelings in her mind " and got so " worked up " that she " shook the children and broke things." She finally felt that she would have to kill both herself and the children. Physical examination showed no abnormalities in the central nervous system or elsewhere.

Blood W.R., negative. M.K.R., negative (15/7/34).

Her mental condition gradually settled down and she was discharged from

hospital on 24/11/34, when it was stated that " she was now probably returned to her normal—an unstable, irrational, self-opinionated woman."

On her return home it was obvious that she had made no real " recovery." She continued to neglect her children, home, and person. She was depressed and unsocial. She refused to eat any food other than that cooked by herself. The children were eventually removed to the care of the N.S.P.C.C. and she became increasingly depressed, agitated, and suspicious. On one occasion she said that a policeman was standing looking at the house when apparently there was no one to be seen. She was admitted to the Maudsley Hospital on 27/9/37. Her mental and physical condition at this time are summarized as follows: " She is apathetic, mistrustful, and slightly paranoid. Her condition is faulty and her memory is very defective, especially for events since 1934. Her powers of retention and her general knowledge are poor. She appears to realize that she is ill but has no proper insight into her condition. Her movements are clumsy, limbs are spastic, and show coarse tremors. The right pupil is irregular and smaller than the left (outline regular). Both pupils react weakly to light, but give normal consensual responses. She is faulty in her habits."

Clinical Investigation of Focal Symptoms by Dr. W. Mayer-Gross

Besides marked signs of general mental deterioration the patient showed symptoms of circumscribed defects. During frequent examinations between 18th and 27th October, 1937, she became more co-operative although she was always slightly perplexed and often bewildered when she did not succeed in any individual test.

Neurological examination revealed rigidity in both arms, especially on the left side; latent paresis of the left arm which tended to drop when the eyes were closed. All deep reflexes were slightly increased on the right side. Adiadochokinesis was present, being more marked on the left side.

Investigation of the visual functions revealed a left-sided defect almost amounting to hemianopia. There was a general impairment of visual attention, especially in the periphery. No colour scotoma was found. Optokinetic nystagmus was negative to the right; the naming of colours was undisturbed as was the selection of named colours. There was a tendency to pick out details from scenic pictures, but no visual agnosia for objects. The patient was able to read the time from a clock.

There was severe finger agnosia. Imitation of finger postures was impossible. The distinction between right and left was abolished.

Visual counting was severely impaired. As regards mental arithmetics, only simple sums and tables could be done correctly; problems such as multiplying 16 by 2 or dividing 26 by 2 could not be accomplished. The reading of numbers was correct, but there was a typical number-writing disturbance in that she wrote, e.g. 311 as 300+11.

She was unable to repeat a rhythm containing more than three elements tapped out on the table.

Investigation of her writing ability revealed literal agraphia especially in letters which are not often used, such as *z*, *qu*, *k*.

Words were correctly spelled, but wrongly written. There was a tendency to perseveration and inability to copy written words which she was able to read.

No object apraxia was found in simple activities, such as using soap, the water tap, etc. She was unable, however, to use a tape measure and failed almost completely in pretending purposeful movements, such as catching a fly, playing the piano, etc. Expressive movements of face and hands were unimpaired.

She was completely unable to copy a square from matches, a simple pattern of coloured mosaics, or a " tower " built from four coloured bricks despite many efforts. Nor was she able to copy a simple drawing. In this and in writing " closing in " was a marked feature.

The investigation thus clearly demonstrated left-sided hemianopia, disturbance of visual attention, constructional apraxia, drawing disturbance, finger agnosia, inability to distinguish right from left, agraphia, and acalculia. All the symptoms were indicative of a lesion in the parieto-occipital region, preponderantly, but not exclusively of the left hemisphere.

Electro-encephalogram (*Mr. Grey Walter*)

Nothing definitely abnormal but occasional rapid high potential discharges from the parietal regions of both sides.

X-ray of Skull.—Normal appearance.

Blood.—W.R., negative (29/9/37).

Cerebrospinal Fluid.—W.R., negative; cells, 1 per c.mm.; protein, 55 mgm. per cent.; Lange, 5532100 (1/10/37).

Cells, 1 per c.mm.; protein, 60 mgm. per cent.; Lange, 55432100 (15/10/37).

Blood counts and urine examination normal.

Discharged to Observation Ward on 19/11/37—" Unimproved."

Admitted to Bexley Hospital on 26/11/37. Her mental state at this time was characterized by extreme confusion. She was completely disorientated for time and place and showed instantaneous amnesia. She thought that she was in the Maudsley Hospital and had been there for 14 months. She stated that she saw her husband (dead for 7 years) on the previous day and had slept with him on that night. She was extremely suggestible and fabricated on the slightest pretext. With a little suggestion she could be made to give the most fantastic accounts of herself, e.g. that the Prime Minister had recently taken her to a dinner and given her an opal ring which was now on her finger (the finger in question being ringless). She was restless and frequently attempted to strip herself and wander about the ward. She frequently sat up in bed saying repeatedly: " I feel sleepy; may I go to sleep? " She held herself rigidly and was resistive to attentions. She was oblivious of personal needs and required constant care and supervision by the nursing staff. On admission her physical condition was in accordance with the facts reported from the Maudsley Hospital. The spasticity of the limbs was especially noted, and the left arm was stated to be more rigid than the right. No definite Plantar response was elicited in either foot, but a definitely " positive " reaction to Oppenheim's test was obtained, and there was a tendency to spontaneous knee clonus.

She remained noisy, restless, and confused. On 26/12/37 she suddenly collapsed, became extremely pallid, and died within a few minutes.

Pathological Investigation

Only the brain was available for investigation. Its weight taken at the post mortem was 975 gm. The meninges were thickened and opaque. The cerebral convolutions appeared to be moderately atrophic, but there was no major circumscribed atrophy. The arteries at the base were normal. On dissection no gross lesion was seen. The lateral ventricles were slightly enlarged.

Microscopic examination revealed changes characteristic of dementia paralytica. They consisted of infiltrations in the meninges and around precapillaries and capillaries of the grey matter with plasma cells, lymphocytes, and occasional mast cells. Furthermore diffuse microglial proliferation, iron deposits in adventitial and microglial cells, and a varying degree of degeneration and outfall of nerve cells were found. These changes were seen in the cerebral cortex, caudate nucleus, putamen, and hypothalamus, whereas they were negligible in the globus pallidus, grey centres of the midbrain, brain stem, and cerebellum.

The iron rection in these various regions was not uniformly positive. Only in the putamen and the caudate nucleus was there a diffuse and even distribution of hemosiderin deposits within the adventitial cells and microglia. In the cerebral cortex strongly positive regions alternated with those in which the reaction was weak or entirely absent. This variation did not correspond to differences of the inflammatory changes. Regions with pronounced inflammation might be entirely free from iron deposits. Since the brain had been in formalin for a considerable time prior to the investigation, it is impossible to say whether the irregularity of the iron reaction was an abnormal feature of the case or merely due to the post mortem action of formalin.

Figs. 1–3 show the appearance of the pathological process in Nissl preparations taken from the frontal, parietal, and occipital regions at the same magnification. It is easily seen that while there was some degree of variation of the severity of the

Fig. 1.—Frontal cortex, Nissl stain. 21×.

lesions in the two former regions the occipital cortex was affected most intensely (Fig. 3, Figs. 4*a* and *b*). The process was particularly severe in the parastriatal cortex, while the calcarine region, though not spared, was less involved. There were further interesting points of difference between the occipital regions and the rest of the cortex. Fig. 3 shows marked inflammatory changes in the deep white matter which was not affected in other regions with the exception of the superficial parts adjacent to the cortex which are commonly affected in the paretic process. Corresponding to the inflammatory changes in the white occipital matter, there was diffuse and patchy demyelination of a moderate degree (Fig. 5), fibrous gliosis (Fig. 6), and lipoidal breakdown products in fixed glial and adventitial cells and only occasionally in mobile compound granular cells. These lipoidal deposits stained brightly with Scharlach R (Fig. 7). No demyelination or formation of lipoidal breakdown products was seen anywhere else in the white matter, while a slight fibrous gliosis of the white matter was found also in other lobes of the brain. Inflammatory changes of the occipital cortex and white matter as well as demyelination and the formation of lipoidal breakdown products was fairly symmetrical on both sides. The demyelina-

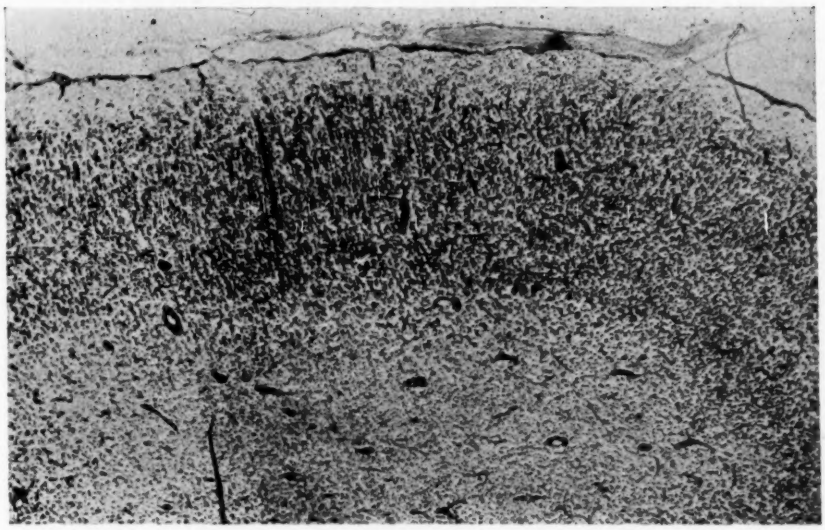


Fig. 2.—Parietal cortex, Nissl stain. 21×.

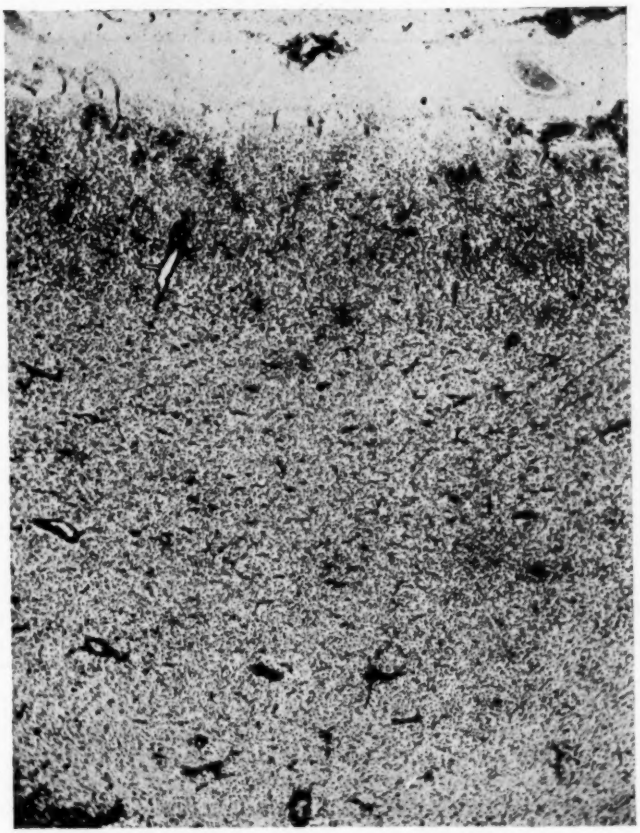
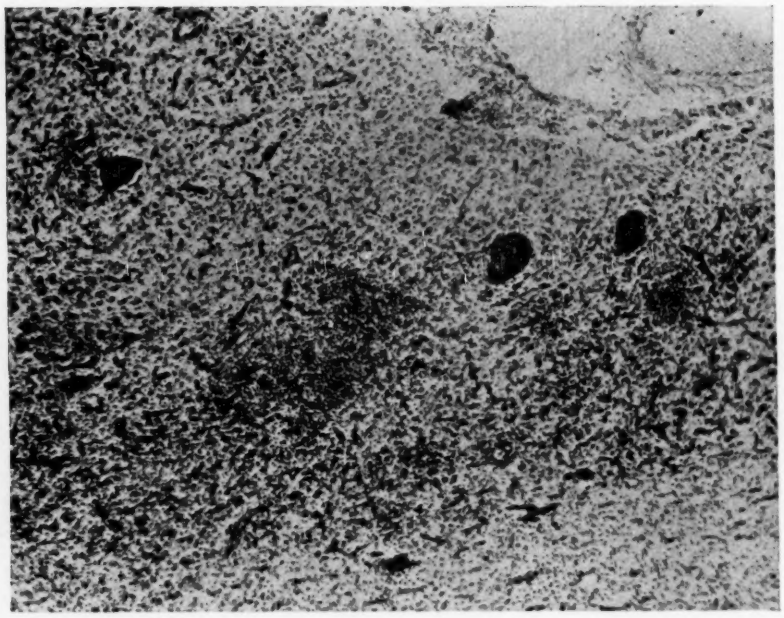
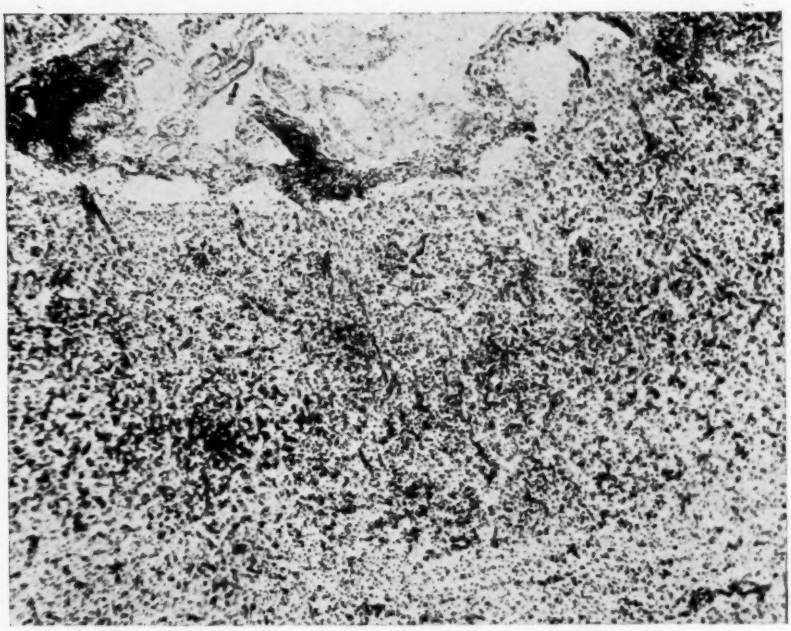


Fig. 3.—Occipital cortex, Nissl stain. 21×. Note especially the marked perivascular infiltration within the deep white matter.



A



B

Fig. 4.—Occipital cortex, Nissl stain. 55×. Showing, apart from perivascular infiltrations, massive cellular accumulations (mainly plasma cells).

tion to some extent involved the visual tract but there were no signs of degeneration in lower levels of the visual pathways.

The difference of the inflammatory changes in the occipital region as compared with other regions was not only quantitative. A significant feature in the occipital

region was the disregard of the plasma cells and lymphocytes for the pioglial membrane. Some plasma cells lying outside the vessel sheaths were seen in other cortical regions, but it was exceedingly rare to find them in such numbers anywhere except in the occipital cortex. Some of the cellular accumulations which Fig. 4 demonstrates were almost entirely composed of plasma cells, and sometimes so densely packed as to simulate a plasmocytoma (Fig. 8) although this was, of course merely a superficial resemblance. In and around such areas the cytoarchitectonic structure of the cortex was more profoundly disturbed than in even the severest cases of ordinary G.P.I. Only a few surviving nerve cells were seen. Apart from these and the numerous inflammatory cells a large number of plump cells and actively proliferating blood vessel elements were the main constituents of the cortical tissue. There was a predeliction of these severe changes for the upper layers although occasionally they also occurred in the deeper layers. Nowhere had a spongiose state developed, but there was a distinct loosening of the texture of the so-called ground

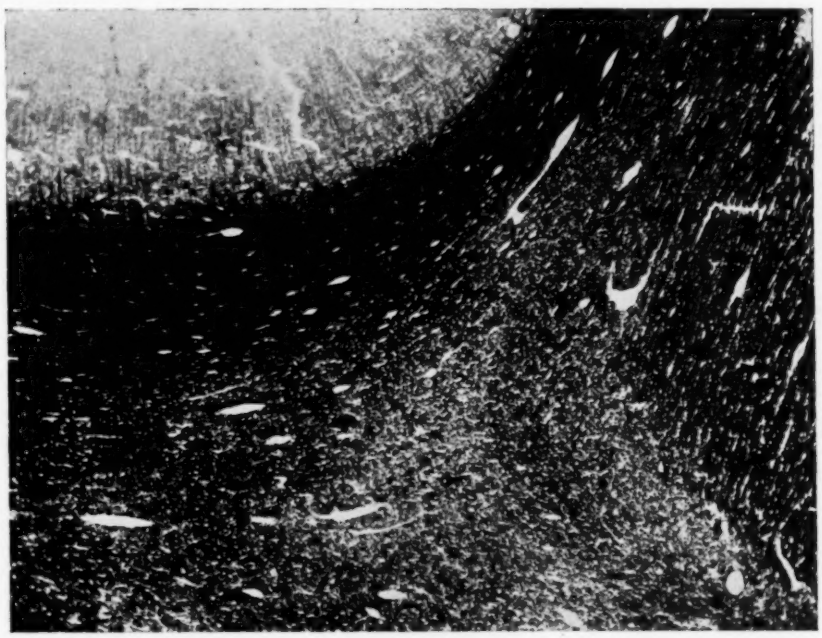


Fig. 5.—Occipital lobe, Weil stain for myelin.

substance. Despite the severity of the destructive process the fibroglial reaction was rather weaker and more irregular here than in the anterior cerebral regions apart from the plump cells which did not contribute appreciably to the production of glial fibres. In view of the general irregularity of the iron rection within the cerebral cortex nothing can be said about its special behaviour within the occipital lobe.

The type of nerve cell degeneration varied a great deal in all cortical regions. Some cells with enlarged pale nucleus, tigrolysis, and dendrites visible for long distances resembled acute swelling. In others the cytoplasm, after disappearance of the Nissl corpuscles, had become vacuolic and seemed to crumble away at the margin of the cell. In still later stages the swollen nucleus became structureless and disappeared. A fair number of nerve cells was seen in which the nucleus was excentric and the cell globular with the tigroid substance displaced towards the periphery or entirely absent. These cells corresponded to what has been described as "Zellblaehung" which is closely related to both retrograde degeneration and the cell change in Pick's disease. This type of cellular degeneration was somewhat more

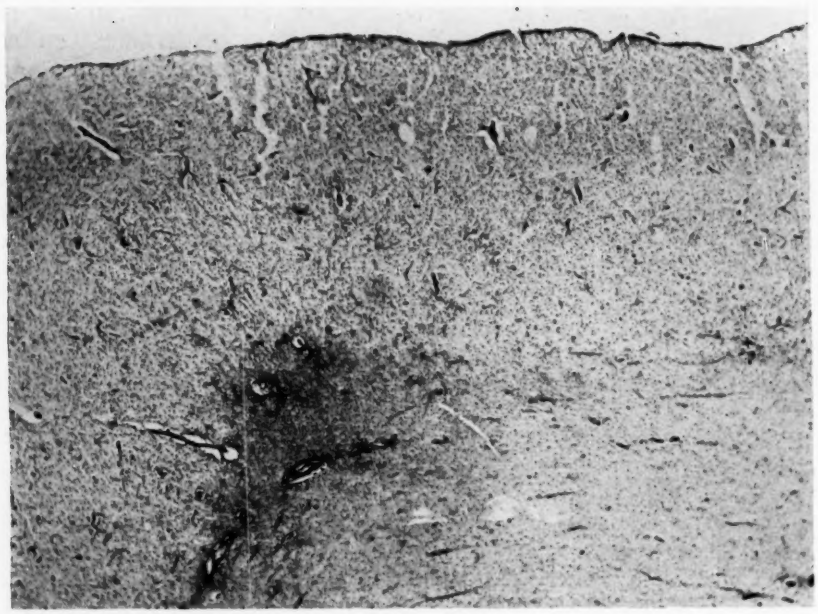


Fig. 6.—Occipital lobe, Holzer stain. Gliosis of the white matter.

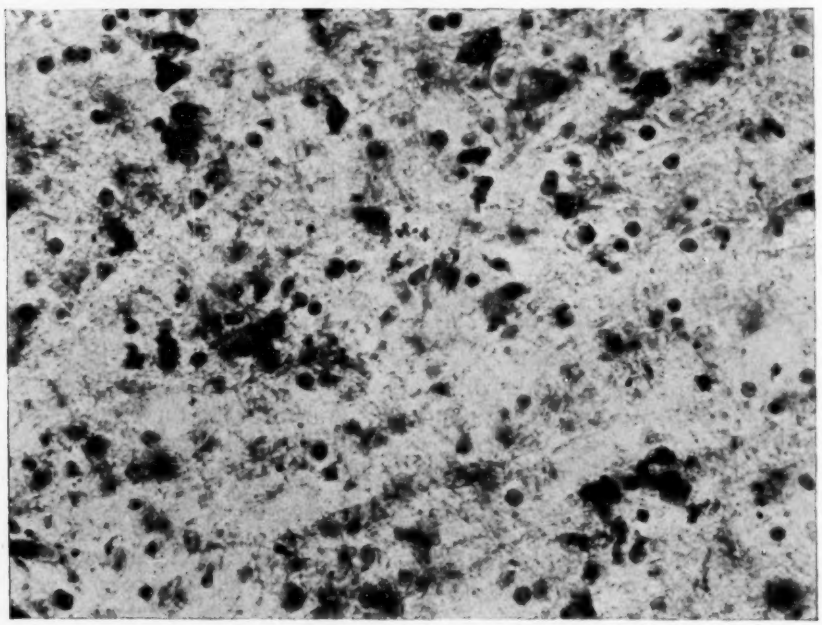


Fig. 7.—Occipital lobe, Herxheimer stain. 350×. Showing lipoidal breakdown products mainly in fixed glial and adventitial cells.

frequent in the severely damaged occipital areas, but it occurred also in other regions of the cortex. Bielschowsky stained slides did not reveal argentophil inclusions in these cells. Ischemic, homogenizing or Nissl severe change were not observed, nor were senile plaques and neurofibrillar thickening found in any part of the grey matter.

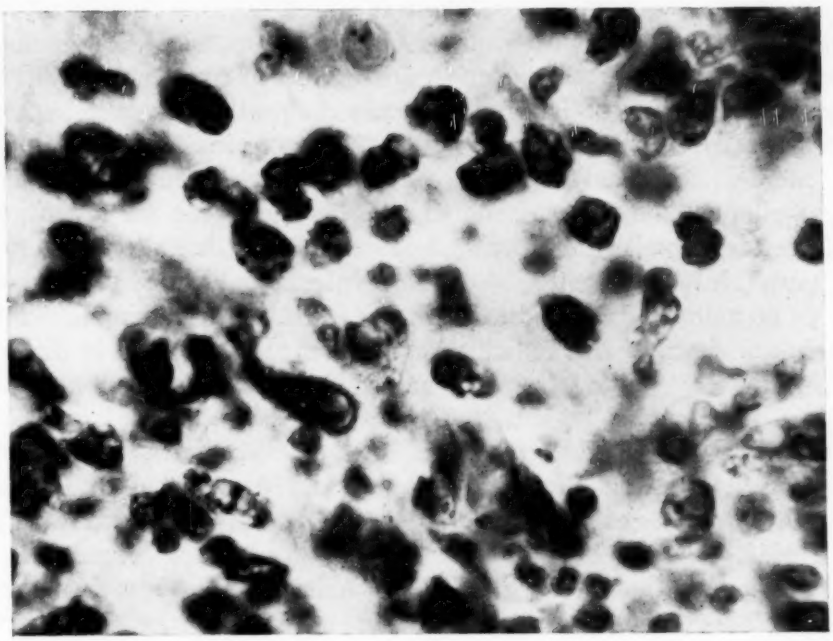


Fig. 8.—Occipital cortex, Nissl stain. 1,100×. Showing a plasma cell accumulation mainly outside the pia-glial membrane.

Numerous blocks from all parts of the cerebral cortex and the white matter were investigated for spirochætes but neither these nor other micro-organisms were found.

No signs of cerebral syphilis independent from the process of general paralysis were found. The frequently marked lymphocytic cell infiltrations around cortical vessels cannot be interpreted as miliary gummata as had been done on similar histological evidence by previous authors.

Discussion

Reviewing briefly the clinical history in the case which we have described, it will be seen that this patient's mental illness extended practically continuously over a period of 6 years (1931–37). Until 1934, when she was able to leave Bexley Hospital, her condition had been regarded as a psychotic reaction occurring in a rather unstable paranoid woman, consequent upon the untimely death of her husband. At this time (1934) there was no evidence of any organic cerebral disease, and the Blood W.R. and M.K.R. were negative. Three years later (1937) she was re-admitted to the Maudsley Hospital, and although the report on her condition, during the interval since her discharge from Bexley, did not suggest that her present condition was other than a relapse of her former psychosis, clinical examination revealed definite evidence of organic cerebral changes. The presence of an Argyll Robertson pupil, the organic

nature of the psychosis which in some respects resembled a Korsakow syndrome, and the serological findings although not entirely typical (Paretic Lange curve and negative Wassermann), suggested that the patient was suffering from general paralysis of the insane, and the subsequent histopathological findings were also in favour of such a diagnosis. Without regard for the atypical distribution and the intensity of the process, the plasma cell infiltration, microglial reaction, and positive iron findings in the cortex and corpus striatum, could indicate no other condition, with the possible exception of a Trypanosome infection which can be disregarded in this case.

A more detailed analysis of the histopathological findings shows that the process, although diffuse, attained its maximum intensity in the posterior parts of the cortex, especially the occipital lobes. This in itself is most unusual. Funakawa (1927) investigating 34 cases of general paralysis found the occipital lobes to be entirely unaffected in seven cases. In the remaining 27 instances there was evidence of inflammation but to a lesser degree than in the frontal areas of the cortex. Similarly one of us (A. J. G.), at Horton Hospital, examined the occipital regions in 74 cases of general paralysis, and found inflammatory changes in 12 cases. In 11 of these, however, the infiltrations were of a mild degree and involved only the parastriatal areas. In the twelfth case the inflammatory changes were more pronounced but not exceeding those in the frontal lobes. The " posterior " distribution of the process in the case under review, together with the localizing clinical manifestations, suggested a possible relationship to the Lissauer type of general paralysis. This hypothesis, however, requires further examination and discussion, because both clinical and pathological findings, at first sight, do not conform to the generally recognized clinico-pathological syndrome associated with the name of Lissauer. Thus although " focal " manifestations pointing to a lesion in the parieto-occipital regions were undoubtedly present (*vide* Dr. Mayer-Gross's report and the result of the electro-encephalogram), convulsions were not reported and various authors, e.g. Merritt and Springlova (1932) have stressed the diagnostic significance of convulsions, especially of the apoplectic variety. Nevertheless it would appear injudicious to exclude a diagnosis of Lissauer's Dementia Paralytica merely on the absence of seizures. The mechanism of convulsions is frequently obscure, and may depend to a considerable extent on the localization of intracerebral disease or injury, rather than on the nature of the process involved. Further, there does not seem to be any instance of Lissauer's Dementia Paralytica quoted in the literature, in which the typical local findings were entirely confined to the parieto-occipital regions. In most cases, at any rate, the occurrence of apoplectic seizures appears to be directly related to damage within, or in close proximity, to the " motor " areas of the cortex. If it be conceded that any case of general paralysis which shows definite localizing signs or symptoms be regarded as belonging to the Lissauer type, then there is ample justification for including our case in that category.

Of even greater interest, however, is the comparison of the pathological findings in this case with those generally observed in the Lissauer type. In the first place there were no localized areas of atrophy but the reason for this

may become apparent by consideration of the histopathological changes. There is no doubt that despite an absence of macroscopic atrophy in the occipital lobes, the process in this region differed significantly from the changes in other areas of the cortex. Elsewhere the inflammatory reaction did not exceed a moderately severe degree, as might be found in the average untreated case of general paralysis. In the occipital lobe the infiltrations assumed massive proportions, invading beyond the piaglial membrane, and involving also to a considerable extent the vessels of the deep white matter. Associated with this intense inflammatory reaction, there was gross destruction of the cortical elements, and areas of demyelinization in the white matter. The presence of numerous " plump " cells is of undoubted importance. Spielmeyer (1922) regards these cells as a criterion of rapid and abundant destruction, and they represent an abortive attempt at glial repair, similar to that found in Schilder's disease, and in cases of softening due to vascular injury. It is impossible to over-emphasize the degree of disintegration which had taken place in the occipital cortex in this case, and the significance of this fact becomes apparent when it is considered in relation to the findings usually described in the areas of local atrophy in Lissauer's Dementia Paralytica. Malamud (1937) expressed the general opinion when he states that status spongiosus is the essential lesion in these atrophic regions. Status spongiosus represents gross destruction, combined with an unsuccessful attempt at glial " repair," and Merritt and Springlova have pointed out that in status spongiosus the glial reaction is at first protoplasmic and later fibrous. The type of localized lesion in our case may at least be regarded as equivalent to status spongiosus on the grounds of localized destruction. It may lack the entire disappearance of the nervous parenchyma and substitution by a glial network, but it is quite feasible to suppose that it may represent a " pre-spongious " state. If the patient had not succumbed at this stage it is easy to imagine that the cortical destruction in the occipital regions would have proceeded to a state of entire disintegration, with more or less complete removal of the products of parenchymal destruction, the further development of the fibrous glial elements, and the subsidence of the inflammatory reaction. The absence of macroscopic atrophy has been noted, but if the condition had been allowed to mature in the way we have visualized, then there is little doubt that areas of local atrophy would have made their appearance in the occipital cortex.

Various theories have been advanced to explain the pathogenesis of Lissauer's Dementia Paralytica and the causation therein of status spongiosus. Lissauer and Storch (1901), and later Alzheimer (1904), considered that the changes within the areas of local atrophy were a direct expression of the process of general paralysis itself. Additional factors have been cited to explain the increased damage in the atrophic areas. Jacobs' (1929) theory that the lesion in Lissauer's Dementia Paralytica were due to organic vascular disease is now largely discredited because organic changes in the vessels are seldom observed. It might be worth mentioning that a variety of clinical syndrome which may simulate Lissauer's Dementia Paralytica is occasionally encountered, and corresponds to the cases described by Jacob. It consists of

the co-existence of general paralysis and meningovascular syphilis. Endarteritis may lead to localizing symptoms and thus present the clinical picture of a Lissauer type. We have studied such a case and made a provisional diagnosis of Lissauer's Dementia Paralytica, but at subsequent histological examination it was obvious that the localizing lesions were the sequelæ of softenings in the white matter resulting from thrombosis in endarteritic vessels.

Fischer (1911) introduced a " toxic " element. Bielschowsky (1920) believed that a circulatory factor, namely, altered permeability of the cortical vessels, leading to a " serous soaking " of the tissues, was responsible. Sträussler and Koskinas (1926) also favoured Bielschowsky's theory, and more recently Merritt and Springlova (1932), following the vasomotor theories of Ricker and Spielmeyer, have postulated a circulatory factor of a rather different type. These authors regard the white matter destruction as the primary condition and suppose that it is caused by functional vascular changes (" atony or spasm ") intimately associated with the very constant occurrence of convulsions, which eventually lead to organic damage. Von Braunmühl (1932, 1933) has described the evolution of status spongiosus in terms of colloid chemistry, believing that an intrinsic factor (" endogenous predisposition ") is responsible for the metabolic changes which lead to its formation. Malamud (1937) agrees with Von Braunmuhl in regarding that the changes are due to a " synäretic " process, but while the latter maintained that the synäresis is endogenous and merely released by the inflammation, Malamud believes that a variety of exogenous factors—toxic, metabolic, inflammatory, and possibly others, are the direct cause of the alteration in the colloid state of the tissues. These theories, based on colloid chemistry, however ingenious and possibly indisputable, appear to render but little help in the elucidation of the problem. It is obvious that changes in the colloidal state of a tissue must take place during its disintegration, but the various factors which have been deemed responsible for the initiation of the destructive process, do not differ greatly from those which have already been under consideration without resorting to expression of their action in terms of colloid chemistry.

In considering the findings in our case in relation to these individual hypotheses, there would seem little doubt that the evidence is in favour of the original view held by Lissauer and Alzheimer. The process underlying the " focal " manifestations was essentially inflammatory—an extreme localized intensification of the " normal " pathological process of general paralysis. We have assumed that it represents an early stage, and the previously recorded findings in cases of Lissauer's Dementia Paralytica have invariably been those of later phases in the disease, when the inflammatory reaction has largely subsided. It is not surprising, therefore, that so many different theories have been evolved to account for the state of localized disintegration which would appear to have little direct relationship to the inflammatory phase. Yet it would be unwise to dismiss these other factors as of no pathogenic importance, because each or all of them may well arise during the course of the inflammatory process. For instance, the " toxic " factor mentioned by Fischer, and the " serous soaking " of Bielchowsky would be almost natural results of such

intense inflammation. Œdema of the tissues, hyperæmia, and endothelial swelling of the vessels would inevitably result in vascular stasis which would then have its added effect. In some cases there is unmistakable evidence of a vascular factor, such as ischæmic cell necrosis, and areas of softening as have been reported by Merritt and Springlova. But such findings are certainly not invariably reported in the cases published in the literature, and were not seen in our case. Of considerable interest in our case was the evidence of inflammation within the deep portions of the occipital white matter. This may well indicate that the white matter changes, considered to be the primary lesion and of vascular origin, by Merritt and Springlova, are also the direct result of the inflammatory process. If a vascular mechanism must also be postulated, then in this case at any rate it is likely to be secondary and not the primary condition. Reference has been made by Smith (1934) quoting Spatz, to " transitional " cases between ordinary general paralysis and Lissauer's Dementia Paralytica. The existence of such cases does not, of course, exclude the possible operation of additional factors, but must surely favour the assumption that the Lissauer type arises directly from the generalized paretic process.

If the inflammatory process itself is to be held responsible for the accentuated local damage in the Lissauer type, then naturally the role of the *Sp. Pallida* must be considered. In view of the negligible findings in the atrophic areas, spirochætes have not been held directly responsible by previous authors. It must be remembered, however, that if the condition has proceeded to a state of atrophy, with more or less complete subsidence of the inflammation, the absence of spirochætes should not necessarily permit any conclusion to be made with regard to their pathogenic insignificance. This would not apply to our case where intense inflammation was still present, but it is universally conceded that the failure to demonstrate spirochætes in about one-third of untreated cases of general paralysis is no proof against their direct action in these instances. It is well known (Jahnel (1918), Hermel (1921), Marinesco and Minea (1913), Levaditi, Marie and Bankowski (1913)) that spirochætes are most abundant in the ordinary type of general paralysis when patients die during paralytic seizures. In the light of this fact it seems strange that all previous authors should have discounted the possible significance of spirochætal action in the Lissauer type, in which convulsions are generally so prominent. We feel, therefore, that the problem of the *Sp. Pallida* in Lissauer's Dementia Paralytica is as yet unsolved and merits further attention.

Summary and Conclusions

The necessity for caution and reserve in arriving at any conclusion on the evidence of one case has not been overlooked, but in this instance there are certain features which enhance its value as a single observation. For reasons which have already been discussed it is believed that an opportunity has arisen to study the Lissauer process at an earlier stage than has hitherto been recorded. The contribution which this case has made towards the elucidation o f t l pathogenetic problem in Lissauer's Dementia Paralytica, is that in this insta n c

at least, the evidence supports the original view of Lissauer and Alzheimer that the circumscribed lesions are essentially due to a local intensification of the paretic process.

Moreover, it demonstrates that the absence of apoplectiform or epileptic convulsions on the clinical side, and of macroscopic atrophy and status spongiosus from the pathological aspect, do not necessarily exclude a diagnosis of Lissauer's Dementia Paralytica. The desirability for a more detailed clinical analysis in cases of general paralysis, such as applied by Dr. Mayer-Gross in this instance, becomes apparent. If such a procedure was universally adopted, it migh well reveal a higher incidence of the Lissauer type and particularly in the earlier stages, than previously supposed.

Acknowledgments

We are indebted to the Medical Superintendents of the Maudsley Hospital and Bexley Heath Hospital for the permission to publish the case and to make use of the clinical records. We owe thanks also to Dr. Nicol for his consent to refer to certain findings in other cases studied at Horton Hospital.

Preparation of the histological specimens and the microphotographs has been done by Mrs. E. Beck working at the laboratory under a Rockefeller Grant.

References

Alzheimer, A. (1904). *Histologische Sudien zur Differential/diagnose der progressiven Paralyse, in Nissl: Histologische und histopathologische Arbeiten ueber die Grosshirnrinde.* Jena, Gustav Fischer, Vol. 1.
Bielschowsky, M. (1920). *J. Psychol. Neurol. Lpz.*, **25,** 72.
Braunmühl, A. (1932). *Z. ges. Neurol. Psychiat.*, **142,** 1.
—— (1933). *Ibid.*, **148,** 1.
Buder, P. (1903). *Allg. Z. Psychiat.*, **60,** 534.
Dalke, M. (1938). *Rev. Asoc. méd. argent.*, **52,** 786.
Divry, P. (1939). *J. belge Neurol. Psychiat.*, **39,** 5.
Fischer, O. (1911). *Z. ges. Neurol. Psychiat.*, **7,** 1.
Funakawa, Y. (1927). *Arch. Ophthal.*, **119,** 270.
Hermel, H. (1921). *Z. ges. Neurol. Psychiat.*, **73,** 419.
Jakob, A. (1929). *Anatomie und Histologie des Grosshirns.* Leipzig, Franz Deuticke, vol. 2.
Jahnel, F. (1918). *Z. ges. Neurol. Psychiat.*, **42,** 21.
Levaditi, C., Marie, A., and Bankowski, J. (1913). *Ann. Inst. Pasteur*, **27,** 576.
Lissauer, H., and Storch, E. (1901). *Mschr. Psychiat. Neurol.*, **9,** 401.
Malamud, N. (1937). *Arch. Neurol. Psychiat. Chicago*, **38,** 27.
Marinesco, G., and Minea, J. (1913). *Rev. neurol.*, **9,** 581. (Vol. **25,** No. 9.)
Merritt, H. H., and Springlova, M. (1932). *Arch. Neurol. Psychiat. Chicago*, **27,** 987.
Ogino, R. (1936). *Jap. J. med. Sci.*, **4,** 23.
Smith, J. (1934). *Med. Times, N.Y.*, **62,** 372.
Spielmeyer, W. (1922). *Histopathologie.* Springer, Berlin.
Sträussler, E., and Koskinas, G. (1926). *Z. ges. Neurol. Psychiat.*, **105,** 55.

ACUTE PULMONARY ŒDEMA WITH HYPOGLYCÆMIC COMA

AN EXAMPLE OF ACUTE PULMONARY OEDEMA OF NERVOUS ORIGIN

F. PARKES WEBER and K. BLUM

(RECEIVED 10TH APRIL, 1942)

THE patient, a man (A. N.), aged 40 years, was receiving 60 units of protamin-zinc insulin daily for his diabetes mellitus, when he was infected with influenza. As a result he fell into a sub-comatous condition, but he recovered quickly with daily 90 units of ordinary insulin and 100 gm. of carbohydrate (porridge), the urine becoming free from sugar and ketone bodies in 3 days. About a week later, on 1st February, 1942, at 6 p.m., after an injection of 30 units of ordinary insulin, the patient complained of a disagreeable feeling of hunger, which was got rid of by 20 c.c. of a 20 per cent. solution of glucose together with a meal of porridge. Six hours after the insulin injection the patient during apparently ordinary sleep fell into a condition of coma, which commenced with typical pulmonary œdema. There were the severest symptoms of hypoglycæmic shock: unconsciousness; extremely contracted pupils which did not react to light; muscular rigidity; restlessness; ankle and patellar clonus; bilateral plantar reflex of Babinski type; psychotic screaming. One might describe the condition as one of " screaming coma " with tetanus-like rigidity of limbs and trunk (opisthotonus). Treatment for the hypoglycæmic coma did not remove the pulmonary œdema, but a hyoscine-atropine injection worked immediately and brought the severe attack to an end, though the patient seemed rather weak for 2 or 3 days afterwards.

Discussion

In the present case there was no evidence of mitral stenosis, coronary sclerosis, myocardial anæmia, arterial hypertension, or any chronic disease of the lungs or cardio-vascular system, and it seems clear that the acute pulmonary œdema must have been of nervous origin. We would compare it to the attacks of pulmonary œdema sometimes associated with epileptic attacks and occasionally constituting the fatal termination. In rare cases of paroxysmal pulmonary œdema (Riesman, 1907, Case 2) cerebral symptoms, such as fleeting aphasia, paralysis of limbs, stupor, or coma, have been associated with the attacks. Shanahan (1908) recorded a number of cases illustrating acute pulmonary œdema as a serious complication of epileptic seizures, and Ohlmacher (1910) described five epileptic cases in which acute pulmonary

œdema constituted the terminal event. Langeron (1925) discussed the case of a woman in whom epileptic crises were regularly followed by an attack of acute pulmonary œdema. One of us (Weber, 1922) would also compare as an analogous phenomenon eclamptic attacks in children during which auscultation of the chest reveals rapid " filling up " with coarse moist râles, passing away when the attack subsides. Such temporary bronchorrhœa in children during eclamptic states is probably due to irritation of the bronchosecretory fibres of the vagus nerve. Moutier (1918) has drawn attention to occasional cases of fatal pulmonary œdema in soldiers suffering from cerebral wounds and the possible danger of adrenalin injections in such cases. Aubertin (1908) experimentally in animals produced convulsions and acute pulmonary œdema by lead poisoning. Bezançon and others (1932) recorded the case of a woman, aged 39 years, with post-encephalitic Parkinsonism, without any cardiac, aortic, or renal lesion, who suffered from recurrent attacks of acute pulmonary œdema, one of which proved fatal. Porter and Greenfield (1941) at a Meeting of the Neurological Section of the Royal Society of Medicine, communicated a case of the " Arnold-Chiari malformation " of the brain-stem with a fatal termination resembling acute pulmonary œdema. It was suggested that the clinical picture was produced by an excessive secretion of the bronchial mucosa glands (? a central autonomic phenomenon) and that the response to atropine was in favour of that view.

Langeron (1925) in the account of his case, above referred to, regarded the attacks of acute pulmonary œdema in that case as a " visceral manifestation of epilepsy." He stated that this " sympathetic epilepsy with visceral manifestations " was from his point of view a spreading out (extension) of the " cortical epilepsy with muscular motor manifestations."

Manunza (1935) has drawn up an elaborate classification of pulmonary œdema of nervous origin. His first class comprises those cases connected with cerebral affections (inflammations, hæmorrhages, tumours, epilepsy), whilst he makes a second class of the cases associated with medullary affections (myelitis, hæmatomyelia, tabes dorsalis) and a third class with affections of the vegetative nervous system and " dysneurotonic " states; his fourth class consists of cases of traumatic nervous origin. Here one might mention that Müller (1891) described an attack of acute pulmonary œdema associated with angioneurotic œdema of the face.

It is certain that the origin of attacks of acute pulmonary œdema varies considerably in different cases and that in most cases multiple factors are at work, but it must be admitted that in some cases an attack may arise in the absence of any true weakness of the right side of the heart (as judged from ordinary and X-ray and electro-cardiographic examination) and without any sudden congestion of the pulmonary blood-vessels, due only to reflex or other disturbance of nervous centres. Hess (1931, 1932, 1933, 1939) lays stress on the probable intervention of nervous reflexes. Impulses, he thinks, which arise sometimes, but not always, in the heart, irritate the vasodilators of the lungs and produce active congestion together with increased transudation into the pulmonary alveoli. In this process, according to his views, the vagus

nerve plays an important part. Wassermann's observation (1933) is interesting, namely, that in some cases pressure on the vagus fibres in the carotid (carotid sinus) can suppress the development of an attack—as it may likewise suppress some attacks of acute paroxysmal tachycardia. Certain observations in experimental pharmacology speak in favour of a vagal causative mechanism in acute pulmonary œdema: vagus irritation from cholines and acetylcholine (Dale, 1914); vagotropic effect of pilocarpin with provocation of an attack of pulmonary œdema; the effect of Sympatol during an attack in diminishing vagotonus through excitation of sympathetic fibres.

We suggest that in our case the attack of acute pulmonary œdema was of pure central nervous origin, due to cerebral œdema and irritation of the vagal nervous system. The clinical symptoms and the rapid response to hyoscine and atropine support this view.

Summary

A case is described of acute pulmonary œdema combined with hypoglycæmic coma, as analogous to the cases connected with epilepsy and other cerebral disturbances. Various nervous origins of attacks of acute pulmonary œdema are shortly considered.

REFERENCES

Aubertin, C. (1908) quoted by Weber, F. P. (1922).
Bezançon, F., Bernard, E., Gennes, L. de, and Delarue (1932). *Bull. Soc. méd. Hôp. Paris*, 1273.
Dale, Sir H. H. (1914). *J. Physiol.*, (P.) **48**, iii.
Hess, L. (1931). *Wien. Arch. inn. Med.*, **21**, 127; (1932), *Deut. Arch. klin. Med.*, **173**, 283; (1933), *ibid.*, **174**, 649; (1939), *Schweiz. med. Wschr.*, **69**, 360.
Langeron, L. (1925). *Pr. méd.*, **33**, 65.
Manunza, P. (1935). *Riv. Patol. nerv. ment.*, **45**, 429.
Moutier, F. (1918). *Pr. méd.*, **26**, 108.
Müller, H. (1891). *Korresp. Bl. schweiz. Ärz.*, **21**, 432.
Ohlmacher, A. P. (1910). *Amer. J. med. Sci.*, **139**, 417.
Porter, R., and Greenfield, J. G. (1941). Not yet published.
Riesman, D. (1907). *Amer. J. Med. Sci.*, **133**, 88.
Shanahan, W. T. (1908). *N.Y. med. J.*, **87**, 54.
Wassermann, S. (1933). *Wien. Arch. inn. Med.*, **24**, 53; *Klin. Wschr.*, **12**, 1615.
Weber, F. P. (1922). *Clin. J.*, **51**, 397.

Addendum

Dr. H. Pullar Strecker (*J. ment. Sci.*, 1938, **84**, 146) knew of only four cases of acute pulmonary œdema occurring as a (most dangerous) complication in connection with the insulin shock therapy for schizophrenia, etc., and referred to the following papers: M. Müller, *Schweiz. med. Wschr.*, 1936, **66**, 929; W. Beiglböck and Th. Dussik, *Schweiz. Arch. Neurol. Psychiat.*, 1937, **39** (Ergänzungsheft), 38; N. Beno, *ibid.*, 149; A. Kronfeld and E. Sternberg, *ibid.*, 187. Dr. Pullar Strecker kindly also gave us later references to the subject: L. A. Finiefs, *J. ment. Sci.*, 1938, **84**, 678 ; S. W. Gillman and D. N. Parfitt, *ibid.*, 718 ; W. R. Thomas and I. G. H. Wilson, H.M. Stationery Office, 1938, 22.

CHEMICAL CHANGES IN THE BLOOD AND THE OCCURRENCE OF URÆMIA FOLLOWING HEAD INJURY

BY

J. N. CUMINGS

* *From the Biochemical Department, National Hospital, Queen Square, London, W.C.*1, *and the Central Pathological Laboratory, Sector* 9, *E.M.S.*

(RECEIVED 14TH MAY, 1942)

URÆMIA as a complication of crush injuries of the limbs is now well known and the histology of the renal lesion has been well described by Bywaters and Dible (1942). The occurrence of uræmia as a complication of head injuries without damage to any other part of the body has not been recognized. This paper describes firstly the results of an investigation begun in 1940 into alterations of various chemical constituents of the blood in patients with head injury only, but in whom no estimate of renal function was made, and secondly the results of renal function tests in 13 patients together with the findings in four cases of uræmia following head injury.

Biochemical Changes in the Blood (excluding Renal Function Tests)

Material and Methods.—Twenty-five patients admitted to various hospitals with head injury were examined. The degree of severity of the injury and the length of time of unconsciousness varied considerably, but the injury was limited to the head in every case. The injuries were related to air raid, road, gun, and explosive accidents. Blood was obtained at varying intervals after the injury, this time factor depending upon the advisability of vein puncture in regard to the clinical condition of the patient, and also upon the fact that patients were transferred from one hospital to another more suited to deal with cranial lesions.

Estimations of the following constituents of the blood were made—serum potassium (Cumings, 1939), sodium (Woelfel, 1938), and hæmobilirubin, plasma chlorides (McCance and Shipp, 1933), and inorganic phosphate (Fiske and Subbarow, 1925). Hæmatocrit readings were made on the first few cases examined but as no significant variations from the normal were found the results are not recorded.

* An expenses grant was received from the National Hospital Research Funds, for which my thanks are due.

Results

Table I gives the results obtained. They are recorded in three groups in order of the severity of the injury. The first group consists of those patients who had a short period of unconsciousness with a minor injury only, the second group of those with fracture of the skull and the last group consists of patients with cerebral contusion as well as fracture of the skull.

TABLE I.—BLOOD CHEMISTRY IN HEAD INJURY

NO. OF DAYS AFTER INJURY	CLINICAL CONDITION.	SERUM HÆMOBILI-RUBIN	SERUM POTAS-SIUM	SERUM SODIUM	PLASMA CHLORIDES AS NaCl	PLASMA INORGANIC PHOSPHATE
2	Slight loss of consciousness No bony injury ..	0·4	—	322·0	549·9	4·4
4	Slight concussion. No bony injury	0·1	16·5	329·9	577·9	—
4	Unconscious. No bony injury	0·3	20·1	310·5	519·5	3·6
6	Slight loss of consciousness. No bony injury	—	24·3	333·8	643·5	5·5
9	Slight unconsciousness. No bony injury	0·3	22·8	320·0	617·7	3·0
9	Slight unconsciousness. No bony injury	0·1	28·1	—	554·6	4·1
10	No unconsciousness. Superficial injury ..	0·15	—	—	580·3	4·0
4	Unconscious. Slight bony injury	0·3	18·9	329·0	503·1	4·5
4	No unconsciousness. Frontal bone fracture ..	0·1	14·1	340·0	549·9	4·0
6	Unconsciousness. Depressed fracture ..	0·3	14·9	338·0	578·0	3·4
11	Unconscious. Occipital fracture	0·1	21·4	314·9	514·8	4·87
12	Unconscious. Frontal fracture	0·1	23·7	323·0	531·2	4·3
1	Severe cerebral contusion ..	0·6	24·1	—	526·5	—
1	,, ,, ,,	0·15	25·6	310·6	514·8	3·5
2	,, ,, ,,	0·2	26·4	294·4	542·8	4·7
3	,, ,, ,,	0·25	—	324·2	538·2	6·4
4	Severe cerebral contusion with cerebral œdema ..	0·2	21·4	—	563·9	—
4	Severe cerebral contusion with cerebral herniation	0·5	14·9	328·8	580·3	—
4	Severe cerebral contusion with cerebral herniation	1·0	23·3	—	551·8	—
4	Severe cerebral contusion	0·3	23·7	300·7	582·0	4·1
4	Subarachnoid hæmorrhage with superficial injury ..	0·3	22·8	301·9	491·4	3·97
6	Unconscious. Fractured base of skull	0·1	20·2	301·3	468·0	4·3
6	Severe cerebral contusion	0·1	—	316·8	585·0	5·4
8	Severe cerebral contusion	0·5	27·7	324·0	444·6	4·7
3	Cerebral irritation. Unconscious	0·2	21·8	300·5	477·4	5·4

(All figures given in mgms. per cent.)

There is some variation from the normal in all substances examined but there is no significant or constant change with the possible exception of the inorganic phosphate content, which tends to be raised in patients with severe cerebral contusion, more especially when the blood is examined several days after the injury. It would be of interest to know if the level of phosphate parallels the degree of demyelination of the cerebral tissue. The blood urea was not estimated in any of these patients. It may be that the raised level of phosphate in some of these 25 patients was associated with renal abnormality and not with demyelination. This is especially so in view of the blood urea levels found in the series to be recorded and also as in uræmia the phosphate level may be raised.

Changes in the Blood and Urine in Uræmia Associated with Head Injury

Material and Methods.—Seventeen further patients with injury limited to the head were investigated. The patients were carefully selected so that only those showing unconsciousness of some hours duration together with a marked degree of severity of cerebral damage were examined. Uræmia developed in four of these patients, three of whom died, and in two of these autopsy was performed. Investigation of the blood was made in all, and the urine was examined in as many patients as was possible, but three of the uræmic patients were incontinent, so making such examination difficult. Serum potassium, sodium and hæmobilirubin, plasma chlorides and inorganic phosphate, blood urea by Archer's modification of Folin and Wu's method (Harrison, 1937), and blood uric acid by a modification of King's *et al* method (1937) were estimated. Urea (Harrison, 1937), *p*H, inorganic phosphate, daily volume, albumen, and centrifuged deposit were estimated or examined for in such urine specimens as could be obtained.

Chemical analysis was performed on the kidneys removed at autopsy and the chloride, total phosphate, and uric acid contents estimated on the cortex and the medulla.

Results

Normal figures for blood urea were obtained in seven of the 17 patients, slightly raised levels in six, and a marked increase in the four patients who developed uræmia. Table II shows the results of the six cases in whom slightly increased blood urea figures were obtained.

The increase in blood urea is not marked but as the patients were young adults the figures are on the high side of normal, and this is confirmed in the one case examined nearly four weeks after the accident, by which time the blood urea had fallen to a normal figure. No other abnormalities were found in the investigations on these patients.

The chemical findings in the four cases of uræmia are given in Table III and short clinical abstracts will be found at the end of the paper.

TABLE II

CASE	NO. OF DAYS AFTER INJURY	BLOOD UREA, MGM. %	PLASMA INORGANIC PHOSPHATE, MGM. %	BLOOD URIC ACID, MGM. %	URINE VOLUME IN 24 HRS. C.C.	URINE UREA, gm. %	URINE INORGANIC PHOSPHATE, mgm. %
M. ..	7 days	44·0 (clearance 88·2%)	—	—	—	—	—
Van P. ..	4 days	43·0	3·97	—	—	—	—
Gi ..	3 days	46·0	3·28	—	446	3·6	12·9
	27 days	25·5	5·5	—	1,652	1·22	41·1
Ga ..	3 days	35·0	3·64	5·2	—	—	—
L.	2 days	45·0	—	—	1,107	1·9	71·6
C.	3 days	60·4	2·25	4·4	407	2·2	110·0

Incontinence of urine was present in three of these patients and in one there was anuria for the first day after the injury, so that urine analysis was difficult to perform satisfactorily. The kidneys of the two patients on whom autopsy was performed showed definite pathological lesions which are being described elsewhere, but which in the main consisted of degeneration of the proximal portion of the tubular epithelium at its point of exit from the glomerulus; in one case there were blood casts in the collecting tubules, features which are quite dissimilar to the changes seen in the kidneys from cases of traumatic anuria.

The most noticeable feature in the blood apart from the raised blood urea was the raised inorganic phosphate content. The urine specimens examined are remarkable for the high rate of excretion of urea with a reasonably concentrated urine, the degree of acidity of the urine, and in one case the low chloride content. The volume passed was about normal as far as could be determined by the degree of bed wetting as judged by a competent Sister.

The mechanism causing the renal lesion in traumatic anuria is unknown, and this is also the case in uræmia following head injury. Shaw Dunn *et al.* (1941) from observations on cases of crush injuries suggested the possibility that uric acid or phosphoric acid might have an ætiological significance, as the site of the renal lesion in their cases of traumatic anuria was similar to the renal lesion caused by these substances in experiments on animals. However, the site of the renal damage is not the same in head injury as in crush injuries of the limbs. Nevertheless, the head injury cases showed a raised plasma inorganic phosphate and in one case a raised blood uric acid level. It is possible that the damaged cerebral tissue liberates a substance containing phosphate, or that there is an alteration of an enzyme system which is concerned with the breakdown of such substances.

It was considered possible that an analysis of the renal tissue might yield interesting and instructive results, hence three normal kidneys and two from the patients on whom autopsies were performed were examined and Table IV shows the results obtained.

It is seen that in the cortex there is no significant difference between the normal and the abnormal kidneys, but the medulla shows a higher phosphate

TABLE III.—CHEMICAL CHANGES IN URÆMIA ASSOCIATED WITH HEAD INJURY

	DATE	BLOOD							C.S.F.		URINE							
		UREA	INORG. PHOSPHATE	URIC ACID	POTASSIUM	SODIUM	CHLORIDE	HÆMOBITI-RUBIN	UREA	INORG. PHOSPHATE	DAILY VOLUME IN C.C.	SPECIFIC GRAVITY	*p*H	UREA	INORG. PHOSPHATE	CHLORIDES	ALBUMEN	CENTRIFUGED DEPOSIT.
Case J.	8.1.40	450	—	—	—	—	339·3	—	—	—	1,132	—	—	—	—	—	Tr.	—
Age 18	9.1.40	560	—	—	—	—	—	—	—	—	1,568	—	—	—	—	—	Tr.	No casts.
Injury, 29.12.40 ..	10.1.40	—	—	—	—	—	—	—	—	—	1,596	—	—	—	—	—	—	—
Died, 13.1.41 ..	11.1.40	472	—	—	23·7	340·5	—	0·3	—	—	1,904	—	—	—	—	—	Tr.	—
Case P.	26.11.41	123	5·36	5·68	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Age 36	27.11.41	141	—	—	—	—	—	—	—	—	(Incontinent)		—	—	—	—	—	—
Injury, 15.11.41 ..	1.12.41	160	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Died, 6.12.41 ..	6.12.41	172	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Case S.	13.1.42	51	2·7	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Age 15	15.1.42	—	—	—	—	—	—	—	92	1·4	—	—	—	—	—	—	—	—
Injury, 10.1.42 ..	17.1.42	223	3·4	—	—	—	—	—	—	—	167	1,040	5·5	3,680	94	36·1	Tr.	No casts.
Died, 19.1.42 ..	19.1.42	368	4·7	—	—	—	—	—	—	—	(Incontinent urine by catheter)						—	—
Case M.	24.3.42	81	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Age 29	25.3.42	86	—	—	—	—	—	—	—	—	—	1,027	4·0	3,900	98·3	—	±	Few hyaline casts.
Injury, 9.3.42 ..	28.3.42	63	—	—	—	—	634·5	—	—	—	—	—	8·0	—	—	—	0	Nil abnormal.
	1.4.42	49	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
	25.4.42	25	—	—	—	—	—	—	—	—	(Incontinent)		—	—	—	—	—	
	Began alkalis by mouth on 27.3.42																	

Figures in mgm. per cent.

TABLE IV.—CHEMICAL ANALYSIS OF RENAL TISSUE

		CASE P.	CASE S.	NORMAL	NORMAL	NORMAL
Cortex	Chloride ..	1·41	0·91	1·3	—	—
	Phosphate ..	0·98	1·09	0·95	—	—
	Uric acid ..	—	0·028	—	0·024	0·034
Medulla	Chloride ..	1·74	0·71	1·49	—	—
	Phosphate ..	0·95	0·77	0·45	—	—
	Uric acid ..	—	0·067	—	0·036	0·036

(Figures in gm. per cent.)

and uric acid content in the abnormal as compared to the normal kidney; however, the figures obtained as yet are too few to be of any definite assistance in demonstrating that either substance is an ætiological factor.

However, there are other points of difference between the cases of traumatic anuria and those described above. Bywaters and Dible state that in those cases adequately examined there was a low urea concentration with a dilute urine. The few examinations of the cases here recorded show a normal urea output in a urine markedly acid. It was thought, therefore, that such patients might be benefited by alkalies and the last patient (Case M.) was given large doses of potassium citrate and sodium bicarbonate by mouth. He responded well and immediately the blood urea began to fall and the clinical condition improved, although he is still suffering from the effects of the cerebral contusion he sustained.

Summary

The results of investigations into chemical changes of the blood and urine following head injury are recorded.

It is shown that plasma inorganic phosphate is raised in severe cerebral lesions and that in a few cases uræmia follows rapidly on cerebral injury. Such patients show raised blood urea and phosphate levels with a normal volume of urine, but with a high excretion of urea in an acid urine. Alkalies caused a clinical improvement in one patient with a raised blood urea.

Alterations in chemical content of phosphate and uric acid were found in the kidneys from two of the patients who died of uræmia.

I am indebted to the members of the Medical Staffs of the hospitals at which the patients were seen, and especially to Mr. Harvey Jackson, F.R.C.S. and Mr. E. B. C. Hughes, and also to Mr. R. Nunn, B.Sc. for technical help.

APPENDIX

CLINICAL NOTES OF THE PATIENTS DEVELOPING URÆMIA

CASE J. Age 18. Air raid casualty on 29/12/40.

On admission to hospital the patient showed signs of shock and had severe scalp wounds only which were treated surgically, and with the local application of M & B 693. There was general improvement for 6 days but then vomiting commenced and

continued for 2 days. The scalp wounds were now found to be infected, and drainage liberated pus.

The tongue was dry, blood pressure raised to 170/120, with a heart of normal size, and the urine contained albumen. He slowly went downhill, becoming comatose and finally died 13/1/41.

A fluid intake of between 1,600 and 2,000 c.c. a day was maintained with a good urinary output. No blood or serum transfusion was given, but intravenous saline and glucose were tried without any improvement in the condition of the patient.

There was no history of any previous renal lesion.

Autopsy was not performed.

(I am grateful to Dr. G. R. Steed for these notes.)

CASE P. Age 36. Road accident, 15/11/41.

The patient was admitted to hospital unconscious with bleeding from the ears and nose, and a slight degree of right-sided hemiplegia. He was incontinent. The heart was not enlarged and the blood pressure 130/90. A fractured skull and, in view of the continued unconsciousness, a subdural hæmatoma were diagnosed, but operation performed on 26/11/41 revealed no blood in the subdural space.

He remained unconscious and showed no improvement until he died on 6/12/41.

At autopsy a fracture across the floor of the right middle fossa was found, but no hæmorrhage was present. No other injuries were found during life or at post mortem.

CASE S. Age 15. Road accident, 10/1/42.

Admitted to hospital unconscious with a slow pulse and some bleeding from the nose and bruising over the back of the head. Pupils were pin-point but reacted to light. Some spacticity of the right side and flaccidity of the left. The C.S.F. was blood stained with slight increase of cells and protein.

He remained unconscious with plantar extensors and with some attacks of spasm in the legs and arms. The condition deteriorated until he died on 19/1/42.

At autopsy there was a fracture across the floor of the middle fossa with a little cerebral œdema, and a small amount of blood over the surface of the brain in the region of the fracture.

CASE M. Age 29. Road accident, 9/3/42.

On admission to hospital was unconscious, restless, and with a bruise over the occipital region and bleeding from the left ear. Still unconscious 11 days later, incontinent, but with no other abnormal neurological signs. Alkalies given on 27/3/42, 8 days later was improving clinically and after 10 days of treatment could obey commands, only slightly restless, and no abnormal physical signs were present.

REFERENCES

Bywaters, E. G. L., and Dible, J. H. (1942). *J. Path. Bact.*, **54,** 111.
Cumings, J. N. (1939). *Biochem. J.*, **33,** 642.
Dunn, J. S., Gillespie, M., and Niven, J. S. F. (1941). *Lancet*, **2,** 549.
Fiske, C. H., and Subbarow, Y. (1925). *J. biol. Chem.*, **66,** 375.
Harrison, G. A. (1937). *Chemical Methods in Clinical Medicine*, Churchill, London.
King, E. J., Haslewood, G. A. D., and Delory, G. E. (1937). *Lancet*, **1,** 886.
McCance, R. A., and Shipp, H. L. (1933). *Chemistry of Flesh Food and their Losses on Cooking.* Spec. Rep. Ser. M.R.C. No. 187.
Woelfel, W. C. (1938). *J. biol. Chem.*, **125,** 219.

ELECTRO-ENCEPHALOGRAPHIC STUDIES OF PSYCHOPATHIC PERSONALITIES *

BY

DENIS HILL and DONALD WATTERSON, Major, R.A.M.C.

From a Psychiatric Unit E.M.S. Hospital, and a Military Mental Hospital

AN *abnormal personality* is one which deviates from its appropriate personality norm. *Psychopathic personalities* constitute a sub-group of *abnormal personalities*. Schneider (quoted by Kahn, 1931) has defined psychopathic personalities as *those abnormal personalities who suffer from their abnormality or from whose abnormality society suffers.* This definition points to a cleavage within the group which is apparent in many classifications, and which is the basis of the division into the bipolar types, inadequate and aggressive, adopted in this paper. A certain amplification is necessary. Psychopathic personalities do not include certifiable mental defectives, psychotics, neurotics, or those whose behaviour disorder is due to demonstrable physical disease.

Henderson (1939) classifies psychopaths into three broad groups, predominantly *aggressive*, *inadequate*, and *creative*. The aggressive group is subdivided into those who injure others, those who attempt self-injury, alcoholic and drug addicts, the epileptoid, and the sex variants. The inadequate group embraces a wide variety of types which have in common ineffectual behaviour. The creative group was formulated to bring together the brilliant but unstable eccentrics.

In this paper Henderson's classification is adopted with three modifications. The group of creative psychopaths is not used, as no clinical material of this kind has been investigated. The aggressives have not been subdivided into smaller groups. The sexual perverts have been divided between the aggressive and inadequate groups, but have also been brought together separately for comparison. This simplified method of classification is used, first because this investigation is largely concerned with the aggressive component of behaviour, second because of lack of time for making elaborate and detailed personality studies.

In the *Predominantly Aggressive* group have been included those psychopathic personalities with a history of either determined suicidal attempts, violence to others regardless of the consequences, repeated destruction of property, or combinations of such kinds of aggressive and impulsive behaviour. These are the patients who describe from early years uncontrollable outbursts of temper, which have almost invariably got them into trouble, either with their

* Read before the Psychiatric Section of the Royal Society of Medicine, March 11, 1942.

relatives or the police or other authority. At times they have insight and are able to discuss their abnormality with fair detachment. At other times they picture themselves as the products of hostile circumstances and the victims of a harsh fate; they are then surly, morose, resentful, contemptuous, and heavily sarcastic. Their hostility may be directed narrowly against a few persons, or against the world at large. Inner tension may be shown by tremor, tachycardia, excessive flushing, and occasionally by a peculiar blocking of self-expression.

These patients rarely apply for treatment voluntarily, but are usually sent to hospital for observation following several acts of violence. Frequent findings in their histories are morbid inheritance, disturbed surroundings in childhood (including bad relationships with parents and siblings), truancy from school, repeated changes of occupation, unsuccessful and often stormy marital careers (out of a group of 20 married aggressive psychopaths, marriage was a failure or markedly unsatisfactory in 13 instances), convictions in civil life for such offences as theft, housebreaking, assault, and drunkenness, and charges in the Services for absence without leave and insulting and violent behaviour.

Special mention should be made of the frequency of head injuries, usually incurred during brawling, boxing, or while resisting arrest. As far as possible, no case has been included in this group unless the history showed markedly aggressive behaviour before any head injury.

The *Predominately Inadequate* group is heterogeneous. It includes purely negative psychopathic personalities with no outstanding or distinguishing features except that they chronically fail in life from having too little energy and drive. This group also embraces diverse types such as the schizoid, hysterical, hypochondriacal, depressive and anxious psychopaths, and the pathological liars. These varieties cannot be illustrated in a short space ; they rarely exist as separate entities, and most patients are a conglomerate mixture. Noticeably irritable psychopathic personalities, showing little or no overt aggression, have also been placed in this group. The criteria separating them from the predominantly aggressive psychopaths are: (1) The suicidal attempts they make are feeble and unlikely to be effective, e.g. swallowing a few aspirins. Usually suicidal threats only are made. (2) Violence against others is often contemplated, but is never practised. (3) Destructive acts are limited to throwing things about, petty incendiarism, etc. These patients know they are hot-tempered, but claim to be able to control themselves. Their life histories differ only in degree, but in marked degree, from those of the aggressive psychopaths.

There are no sharp lines between psychopathic personalities and the other mental disorders. Anxiety and hysterical symptoms are common among psychopaths, but a distinction is drawn between neurotics and psychopathic personalities, " in that the symptoms of the latter appear in behaviour, of the former more often in feelings and physical complaints " (Menninger, 1938). Psychopaths often complain also of depression, but this is usually shallow, rapidly variable, overshadowed by irritability, and not accompanied by retardation. Moreover, expression of guilt feelings tends to be replaced by expression of resentment, contempt, envy, and hate.

Clinical Material

The clinical material on which this investigation was based was drawn from four sources: a Military Mental Hospital, the Neurological Department of an Emergency Hospital, certain psychiatric out-patient departments, and in a few cases from out-patients sent directly for E.E.G. by Unit M.Os. It is selected material and does not represent a random sample of psychopathic personalities. It is largely made up of male personnel from the Services. The ages range from 15–51; 90 per cent. of the patients were between 20 and 30 years of age.

Histories have been obtained from the patients themselves, often supplemented by information from relatives, and in a small number from social workers' reports. Service cases are also accompanied to hospital by a report on behaviour from the Unit M.O. or C.O. As many of these patients are not always truthful, some of the histories we have obtained are not as reliable as we would have wished.

Table 1 shows the distribution of this material between the sub-groups. The " mixed " group of 24 patients includes those cases in which neurosis, psychosis, or epilepsy is superimposed on an abnormal personality; 16 of this group showed overt aggression. Only first-degree relatives (i.e. parents or siblings) have been included in the tabulated data showing abnormal family histories.

The control material of presumed-healthy persons was drawn from three sources: R.A.M.C. staff at a Military Mental Hospital, and staff and surgical patients of a general hospital. The clinical investigation of these controls was less thorough than that of the patients, but attention was paid to offences in civil life or in the Army, head injuries, fits and faints, irritability, impulsiveness, and aggressive behaviour.

TABLE 1

SUB-GROUP	NO.		NO.	TOTAL	MORBID FAMILY HISTORY PER CENT.	PATIENTS
Aggressive psychopathic persons..	77	Without recidivism	66	93	44=47	Showing marked overt aggression.
		With recidivism ..	10			
		With perversion ..	1			
" Mixed " ..	24	With overt aggression	16			
		Without overt aggression	8	58	22=38	Showing little or no overt aggression.
Inadequate psychopathic persons.	50	With perversion ..	7			
		With recidivism ..	5			
		Without recidivism	38			
TOTAL PATIENTS			151	151	66=44	
CONTROLS				52		

Historical Introduction

Abnormalities in the electro-encephalogram can be divided into two main groups: (1) where the rhythms are too fast, and (2) when they are too slow. The normal range of dominant or alpha rhythm is from eight to thirteen cycles. There are wide individual variations in the voltage, frequency, and in the time during which the dominant rhythm is present. In some persons dominant rhythm makes up 95 per cent. of the record, in others only 5 per cent.; occasionally the dominant rhythm is of extremely low voltage, and very infrequently there is no dominant rhythm at all. Though in the present stage of knowledge all these variations must be regarded as within the normal range, it has been suggested that a relationship might exist between the dominance of alpha rhythm and personality traits. The results of such investigations have not been very convincing. Saul, Davis, and Davis (1937), using a Freudian interpretation of personality, found that persons with, to quote them, " a freely indulged in drive to activity, independent aggressive social leaders, doers in reality rather than intellectual sublimation, and personalities who dream of attacking and stealing the power, potency or ability of others " tend to have few alpha waves, i.e. a poor dominant rhythm. The opposite type, whom they describe as passive, dependent, and receptive, the men in their opinion having passive homosexual trends, have many alpha waves, i.e. a good dominant rhythm. Gottlober (1938), favouring a Jungian classification, found a relation between extraversion and a dominant alpha rhythm. He was unable, however, to correlate the introverted type with few alpha waves. Lemere (1936), on the other hand, has correlated the schizoid personality with poor alpha rhythm and the cycloid personality with a good one. Unfortunately, it does not appear possible to associate Saul's psychoanalytical personality classification with the psychiatric interpretations of Lemere, but the latter correspond well enough with those of Gottlober. It is interesting that Gottlober found an association between the cycloid personality and a good alpha rhythm, but no such association in the case of the schizoid personality. This is paralleled by other psychophysical studies, e.g. by the finding that there is an association between cycloid personality and pyknic physique, but only a doubtful one between schizoid personality and a leptosomatic physique.

Berger (1936), who believed that the electro-encephalogram in the schizophrenic and manic-depressive psychoses was normal, remarked on the poor alpha rhythm in the former, but considered this and the predominance of high-frequency potentials also present as evidence of emotional tension. Hoagland, Rubin, and Cameron (1937), using a quantitative assessment of abnormally slow waves (the Hoagland or delta index), found that this was higher in schizophrenics than in normal controls. MacMahon and Walter (1938) criticized this on the ground that eye-movement artefacts, which would increase the index, were very common in schizophrenics.

Imagery-type in schizophrenia was investigated by Rubin and Cohen (1939) who used another quantitative assessment—" the per cent time alpha." This is simply the number of dominant waves with a frequency over seven per second in five metres of record. They described a greater homogeneity among schizo-

phrenics than among normal controls, and in those with tactual temperature imagery a significantly lower " per cent time alpha." They suggested a correlation between this finding and Cohen's work (1938) on the change from auditory to tactual temperature imagery in schizophrenics and accounted for it by suggesting that it was part of the phenomenon of narcissistic regression or, as they put it, " a restriction of experiencing from the outside world . . . and the orientation of imagery becoming mainly concerned with the inside world, i.e. that of the body." This interesting psycho-biological approach cannot, unfortunately, be supported, and recently Walter (1942) has suggested that the flat, low-voltage rhythms seen in some schizophrenics may be related to changes in the electrical resistance of the meninges and scalp and be independent of the cortex itself.

It is agreed by most workers that from 5 to 10 per cent. of normal people have electro-encephalograms which fall outside the limits of an arbitrary norm. The view that cortical dysrhythmia (a term synonymous with abnormal E.E.G. for the purposes of this paper) is itself a constitutional defect has had support in the work of Lennox, Gibbs, and Gibbs (1940) on the relatives of epileptics. They found that 60 per cent. of the relatives had dysrhythmia and that of 35 per cent. of epileptic children, both parents were abnormal, both being normal for only 5 per cent. The writers suggest that dysrhythmia may be a dominant trait which is possessed by 12 per cent. of the population who are predisposed to epilepsy or to some allied disorder, either themselves or in their offspring. Episodic behaviour disorder associated with an increase of dysrhythmia in epileptics has been described by Putnam and Merritt (1941), but as far as we can ascertain from the literature, such behaviour *without epilepsy* but *with dysrhythmia* has not been described in adults. Jasper, Solomon, and Bradley (1938) were the first to report abnormal E.E.Gs. in behaviour problem children. These abnormalities are very similar to those found in the psychomotor equivalents of epilepsy, and the children, by their irritability, tempers, egocentricity, and hyperkinesis, are in some respects reminiscent of the epileptic personality. There appears, however, to be no clinical evidence that these children become epileptic. Lindsley and Cutts (1940) have shown that nearly 80 per cent. of behaviour problem children have abnormal E.E.Gs. and that the percentage abnormal in constitutionally inferior children is hardly less. (Under the term " constitutionally inferior " they place children with poor heredity whose problems were predominantly social, economic, or medical.)

Williams (1941*a*) has shown that 26 per cent. of 148 mixed psychoneurotic patients had abnormal E.E.Gs. Apart from this, epilepsy, and the behaviour problem children, the investigation of functional psychiatric conditions by the electro-encephalograph has proved disappointing. The workers who have described finer variations within the normal range are now exposed to the criticism that a considerable number of uncontrolled and probably uncontrollable chemical and psychological factors may be influencing their results. In addition to the electrical resistance of the supporting tissues, the *p*H, oxygen and CO_2 tensions, and the glucose concentration of the cerebral blood are among the known factors which must be considered. On the psychological side, the state

of attentiveness or relaxation, anxiety, and the special meaning which sensory stimuli may have for the patient must be considered when the dominance of alpha rhythm is assessed.

For these reasons, when investigating the electro-encephalograms of psychopathic personalities, we have recorded only abnormalities which lie outside the range of normal and have made no attempt to correlate personality with " per cent time alpha," frequency, voltage, or dominance of dominant rhythm, or the responsiveness of the latter to inhibitory stimuli.

Technique

The apparatus used was three ink-writers motivated by a standard three-channel Grass amplifying unit. The amplifiers were linear from 3 to 50 cycles. The high-frequency filters were kept at position " 3," which is that used by other workers with this standard apparatus (Williams, 1941*a*). The patient sat at ease in a small earthed wire cage and was under continuous observation for eye, scalp, and other movements. The records were taken with the eyes shut, but it must be admitted that, although the environment remained fairly constant, not all the psychological factors tending to disturb relaxation could be controlled. For example, in some instances the patients were brought for the test under close arrest.

The electrodes were small, silver tubes, covered with saline pads, held to the head by means of an open-mesh rubber cap (Walter, 1937). Bipolar electrode placement was used in every case. The usual method was to place four electrodes on widely separated areas of the head, two on each hemisphere. Where more accurate localization of abnormality was attempted, the electrode placement advocated by Gibbs and Gibbs (1941) was used. The latter has, however, the disadvantage that it is impossible to say whether rhythms are bilaterally synchronous. By these methods, there were 20 to 25 minutes of actual recording, which also includes 3 minutes of voluntary hyperventilation. The record is observed for a further 3 minutes after the end of hyperventilation.

Criteria of Abnormality

For our purpose, the following abnormalities were accepted as criteria. They are certainly not the only ones detectable in the E.E.G. For instance, a variability in the frequency of dominant rhythm more than ± 1 cycle is almost certainly abnormal. No attempt to investigate the faster frequencies has been made, for the reason that no check could be kept on the chemical and psychological factors at the time of taking the records. Excessively slow waves were the only abnormalities accepted, except specific wave forms such as spike and wave complexes and the phenomenon which is associated with the aura of grand mal.

Resting Record

1. A dominant rhythm with a frequency of less than 8 per second.
2. Bursts of two or more waves having a frequency less than 7 per second and a voltage more than half that of the dominant rhythm.

3. Series of waves with a frequency of 14 or more rising in voltage to over half that of the dominant rhythm (the grand mal phenomenon).

4. Spike and wave complexes (the petit mal phenomenon).

5. Isolated random waves at 6 per second or less, with a voltage equal to or more than that of the dominant rhythm, provided such waves are repeated from the same cortical area.

Hyperventilation

Each patient was induced to hyperventilate for three minutes. This rather long period was used because many psychiatric patients will not co-operate with full ventilation. It is considered that the longer period may to a certain extent compensate for the deficient depth of breathing in the production of the temporary alkalosis. The significantly abnormal waves, apart from spike and wave complexes, are those with a frequency of 2–3 per second and a voltage over 100 microvolts, which persist after the hyperventilation has ceased. The typical abnormal response is one in which the rhythms, having started to return to normal, are suddenly interrupted by a paroxysmal burst of slow, high-voltage waves, usually from 8 to 15 seconds after the end of hyperventilation. In cases where slow, high-voltage waves persist continuously for more than 20 seconds after the hyperventilation, the response is also regarded as abnormal.

Where a decision as to normality, either in the resting record or on hyperventilation, could not be reached, the patient was re-examined after at least four hours starvation, as this tends to accentuate doubtful abnormalities.

Results

Of the total group of 151 patients, 73 or 48 per cent. had abnormal E.E.Gs. Of these, 20 or 13 per cent. were abnormal in the resting record *only*, and 22 or 15 per cent. after hyperventilation *only*. Thirty-one patients, or 20 per cent., showed abnormalities both at rest and after hyperventilation. In the control group of 52 individuals, 8 or 15 per cent. had abnormal E.E.Gs., and of these 6 were abnormal at rest *only* and 2 showed the twin abnormality: at rest and on hyperventilation. None of the controls showed the abnormal hyperventilation response alone. Fourteen of the patients and three of the controls had E.E.Gs., the normality of which remained in doubt. In these cases, the uncertainty was due almost entirely to irregularities in the resting record. Table 2 compares the total group of patients with the controls. The finding that 15 per cent. of the controls were abnormal is higher than that given by other workers. Lennox, Gibbs, and Gibbs (1940), whose criteria are similar, state that 10 per cent. of their controls were abnormal. Since this investigation was made, one of the abnormal cases has admitted to previous fits and another has admitted to having had a head injury. The selection of normal controls, by the elimination of those who have had head injuries and of those who at any time suffered from faints or fits, is obviously important. In the search for the normal control, however, factors other than head injury and fits must now be considered. The control material of Lennox, Gibbs, and Gibbs was mainly

composed of physicians, technicians, and students, which suggests some degree of selection. D. Williams (1941*a*) has recently shown that the percentage of abnormal E.E.Gs. in highly selected flying personnel who have completed their flying training is only 5 per cent., while in R.A.M.C. personnel it is 10 per cent.

TABLE 2

	POSITIVE				DOUBTFUL			
	PATIENTS (151)		CONTROLS (52)		PATIENTS (151)		CONTROLS (52)	
		PER CENT.		PER CENT.		PER CENT.		PER CENT.
E.E.G. positive rest only	20	13	6	11·5	13	—	2	—
E.E.G. positive hyperventilation only	22	14	0	—	1	—	1	—
E.E.G. positive rest + hyperventilation	31	21	2	3·5	0	—	0	—
TOTAL	73	48	8	15	14	9	3	5

An investigation of the personal and family histories of our control material has been made, as far as this was possible. According to the sources, the material can be divided into three groups: (1) R.A.M.C. personnel from a mental hospital, (2) lay and medical staff from an E.M.S. hospital, and (3) surgical patients. The R.A.M.C. personnel showed the greatest number of abnormal E.E.Gs. The histories of the four men with positive and of one man with a doubtful E.E.G. are informative. As already stated, one has admitted to having had fits; he is also regarded as moderately aggressive and irritable, and had suffered a head injury earlier in life. Of the four other abnormal controls, one was recently on a civil charge for threatening behaviour, another on a military charge for insolence, and another had twelve charges for inefficiency recorded on his military crime sheet. All four were regarded as showing varying degrees of aggressiveness, irritability, and impulsiveness. Only one control with an abnormal E.E.G. in this sub-group had normal personal and family histories. Among those members of the R.A.M.C. control group who had negative E.E.Gs., none had been on more than minor charges in the Army and none for insolence or violent behaviour. Among these there was, however, one man who was regarded as an aggressive psychopath and perhaps an epileptic. He had suffered three head injuries. Another normal control, regarded as slightly aggressive and irritable, had been on two charges for aggressive conduct when he was a boy, but his conduct since then had been good.

Similar information from the surgical group is, unfortunately, not available and, while the E.M.S. hospital staff group were not assessed as the result of personal interviews, the results from a written questionnaire have been obtained. The only person admitting quick temper had a doubtfully positive E.E.G.

Placing the three groups in order of abnormality, one finds R.A.M.C. personnel from the mental hospital highest, E.M.S. staff next, and surgical patients with the lowest degree of abnormality.

As already stated, for the purposes of classification the patients have been divided into 66 predominantly aggressive psychopaths, 38 predominantly inadequate psychopaths, 5 cases of delinquencey without other psychopathic traits, 8 cases of sexual perversion, and a mixed group of 34 patients in whom aggressiveness, epilepsy, delinquency, perversion, schizophrenia, or cyclothymia occurred in various combinations. Table 3 gives the distribution of E.E.G. abnormality throughout the major groups. Out of 66 predominantly aggressive psychopaths, 43 or 65 per cent. were abnormal, and out of 38 predominantly inadequate psychopaths, 12 or 32 per cent. were abnormal. The five purely delinquent patients were normal, as were seven our of eight cases of sexual perversion. Analysis of the mixed group (Table 4) shows that only one of 11 cases of epilepsy with aggression had a definitely normal E.E.G. The three aggressive psychopaths who developed schizophrenic syndromes had normal E.E.Gs. Of the ten aggressive psychopaths who were also delinquent, five had abnormal E.E.Gs. It is apparent that there is a significant difference in the percentage of dysrhythmics between the inadequate and aggressive groups and the controls and also between the inadequate and aggressive groups themselves. The inadequate group has twice as many abnormal E.E.Gs. as the controls, and the aggressive group four times as many. It is necessary to examine (1) the types of E.E.G. abnormality within the two groups, and (2) the influence of any factors likely to have a bearing on the psychopathic state or on the E.E.G. Such factors are head injury, epilepsy, and the family history.

TABLE 3

	TOTAL	E.E.G.				TOTAL ABNORMAL	
		POSITIVE			DOUBTFUL		
		REST ONLY	HYP. ONLY	REST + HYP.			PERCENT.
Aggression	66	10	14	19	4	43	65
Inadequacy	38	3	3	6	6	12	32
Delinquency	5	0	0	0	1	0	—
Sexual perversion ..	8	1	0	0	0	1	—
Mixed	34	6	5	6	4	17	50
Controls	52	6	0	2	3	8	15

Type of Abnormality

As Walter (1942) has pointed out, it is probable that the voltage of cortical rhythms when obtained from the scalp, being subject to variations of resistance

in the supporting tissues, is not necessarily significant of any vital activity of the cortex itself. It is fairly generally agreed, however, that the voltage of rhythms, relative to one another in the same record, has a significance. Thus in epileptics, bursts of slow waves with a voltage higher than that of the dominant rhythm are commonly seen and easily detected. In other epileptics, slow rhythms equal to, or less than, the dominant in voltage are seen and the E.E.G. is still unquestionably abnormal. The difficulty arises in deciding how great the voltage, relative to the dominant, an abnormally slow rhythm must have to be regarded as pathological. When examining a record one observes that there is a threshold voltage above which slow frequencies stand out as having an abnormal appearance. As already stated, the voltage which has been accepted in this investigation, and which we believe is accepted by most other workers in this country is that which is more than half the voltage of the dominant rhythm. While it must be admitted that this is an arbitrary standard, the percentage abnormality among the controls, though certainly higher than that given by other workers, compares not unfavourably.

TABLE 4

	TOTAL	E.E.G.				TOTAL ABNORMAL
		POSITIVE			DOUBTFUL	
		REST ONLY	HYP. ONLY	REST + HYP.		
Epilepsy + Aggression ..	11	2	2	5	1	9
Epilepsy + Perversion ..	1	1	0	0	0	1
Aggression + Delinquency ..	10	1	2	2	3	5
Aggression + Schizophrenia	3	0	0	0	0	0
Aggression + Trauma ..	2	1	0	0	0	1
Aggression + Cycloid ..	1	0	0	0	0	0
Inadequacy + Delinquency ..	6	1	0	1	0	2

The most characteristic abnormality of the resting record in this series was the presence of a 4–6 cycle rhythm, with a voltage slightly less than that of the dominant. The waves have a fairly smooth, regular form and are seen in bursts of three to six at a time. They are repeated at varying intervals throughout the record. In some cases, this abnormal rhythm has a voltage greater than that of the dominant and in many was equal to it. In 11 out of 51 abnormal resting records, three-cycle rhythms were seen and these, in the sense that they were more easily localizable, were comparable to Walter's delta foci in epileptics.

The importance of localization has been stressed by Walter and also by Jasper and Kerschman (1941) in their recent work on the classification of epilepsies. In 35 out of the 51 patients with abnormal resting records, it has been possible to form an opinion as to the probable site of origin of the abnormal potentials. In 25 cases, the rhythms were found in the post-central regions;

of greater interest perhaps is that in 26 the rhythms were bilaterally represented. These rhythms are not usually truly synchronous, but nearly so, and the possibility of " mirroring " by the opposite cortex of a discharge on one hemisphere cannot always be excluded. But as Jasper and Kerschman (1941) has pointed out, in such cases the false focus is usually of lower voltage and more irregular in form. This question in our series cannot at present be decided.

The question next arises as to whether there are any differences in the type of abnormality between the two main groups of patients. As Table 2 shows, while only 10 of the aggressive group had abnormal resting records *alone*, a total of 33 out of 66 had the abnormal response to hyperventilation, and 19 of these were also abnormal at rest. The comparable figures for the 38 patients of the inadequate group were 3 abnormal at rest *only*, 9 abnormal on hyperventilation, of whom 6 were also abnormal at rest. Taking now all the aggressive patients, irrespective of associated epilepsy, delinquency, or psychosis, and comparing these with all the inadequate patients, or more strictly speaking the non-aggressive, we find that of 58 dysrhythmic aggressives 14 or 24 per cent. were abnormal at rest *only*, and that of 16 dysrhythmic non-aggressives, 6 or 37 per cent. were abnormal at rest *only*. There is, therefore, the suggestion that the abnormal resting record, as a single factor, plays a greater part in the dysrhythmia of the non-aggressive group than it does in the aggressive group. As will be pointed out later, this is probably due to the greater incidence of past head injury in those inadequate patients who have positive E.E.Gs.

The abnormal response to hyperventilation has a very typical character and rarely gives rise to doubt when it is present. The 3-cycle smooth waves of high voltage appear either as a continuous series or in bursts of 3–6 at a time. Their persistence for more than 20 seconds after the cessation of hyperventilation or, as is more frequently the case, their re-occurrence after the record has started to return to normal constitutes the abnormality.

The induction of alkalosis by voluntary hyperventilation is now the classical method of producing the spike and wave complexes of petit mal. In only one instance has a series of these complexes occurred and this case was known to be epileptic. The production of a 3-cycle rhythm of high voltage has usually been regarded as the indication of an abnormally unstable cortex, and this finding has suggested a constitutional liability to the epileptic phenomenon. While it is certainly true that very many epileptics show this abnormality, Williams (1941) has demonstrated the abnormal response in a high percentage of chronic post-traumatic states. That conditions other than epilepsy can induce the abnormal response is further supported by an investigation of Hill and Sands, as yet unpublished, on the effects of induced convulsions on the hyperventilation response. The latter is definitely facilitated in some patients by a number of induced fits. It is therefore suggested that while abnormalities in the resting record may consist of a number of as yet unknown entities, the hyperventilation response is a non-specific effect, merely indicating an abnormally functioning cortex. This view is supported by the comparable percentage of hyperventilation abnormality within the total dysrhythmic groups. Thus, 77 per cent. of the total aggressive dysrhythmics, 75 per cent. of the total

inadequate dysrhythmics, and 65 per cent. of the dysrhythmic mixed cases showed the abnormality.

The examination of single traits, extracted from the total material, is of interest (Table 5); the finding that four times as many aggressive psychopaths have dysrhythmia as the controls is certainly significant. As the numbers in this further analysis are so small, no such significance can be claimed, but they further support the finding that aggressive psychopathy is associated with an abnormal E.E.G. They suggest that where epilepsy is also present the figure of 65 per cent. dysrhythmic is still higher. Where delinquency exists alone, 16 per cent. are abnormal—a figure comparable with the controls—but when aggressive delinquency is examined, half the patients have dysrhythmia. The lack of association between delinquency and dysrhythmia is further supported by the finding that its presence has no influence on the percentage dysrhythmic among inadequate psychopaths.

TABLE 5

	TOTAL	NUMBER DYSRHYTHMIC	PER CENT. ABNORMAL
AGGRESSION	93	58	62
With Epilepsy	11	9	81
Without Epilepsy	82	49	60
EPILEPSY	12	10	83
With Aggression	11	9	81
Without Aggression	1	1	—
DELINQUENCY	22	7	32
With Aggression	10	5	50
Without Aggression	12	2	16
INADEQUACY	44	14	32
With Delinquency	6	2	33
Without Delinquency	38	12	32
SEX PERVERSION	8	2	25

Within the aggressive group itself, a division between mildly aggressive, including those only aggressive to self, and severely aggressive, including those with homicidal attacks, has been made. Table 6 shows the results of such a

TABLE 6

	E.E.G. POSITIVE			TOTAL ABNORMAL	PER CENT. ABNORMAL
	REST ONLY	HYP. ONLY	REST + HYP.		
AGGRESSION (66):					
I Aggression + (49) ..	7	10	12	29	59
Aggression ++ (17) ..	3	3	6	12	70
AGGRESSION (93)*:					
II Aggression + (67) ..	11	11	18	40	59
Aggression ++ (26) ..	4	7	7	18	69

* Total group of aggressives, irrespective of epilepsy, delinquency, trauma, etc.

classification with relation to the incidence of abnormal E.E.Gs. It indicates a tendency for the more aggressive group to have a higher percentage of dysrhythmics. The second part of the Table, in which the results are given for all patients, irrespective of epilepsy, delinquency, trauma, etc., who have shown the aggressive personality disorder, indicates that this tendency is real and is associated with aggressiveness alone. The findings in this part of the Table are the same as when aggressiveness is examined alone.

The Influence of Head Injury

Williams (1941*b*) has shown that the E.E.G. may remain abnormal for many years after a head injury and has demonstrated a relationship between E.E.G. abnormalities and the severity of the injury, as judged by the length of post-traumatic amnesia. It has not been possible in this series to judge the severity of the injuries, as the majority have occurred many years previously, usually in childhood. Of the total group of 151 patients, 23 aggressive psychopaths and seven inadequate psychopaths had had head injuries. Ten of the aggressives and four of the inadequates had positive E.E.Gs. (Table 7).

TABLE 7

	TOTAL	E.E.G.		
		POSITIVE	NEGATIVE	DOUBTFUL
AGGRESSION:				
With head injury..	23	10	11	2
Without head injury	63	43	15	5
INADEQUACY:				
With head injury..	7	4	3	0
Without head injury	36	10	21	5

It can be seen from this Table that in the inadequate group, of the patients with probably normal E.E.Gs., 10 per cent. had head injury, while the patients with abnormal E.E.Gs., 28 per cent. had had head injury. In the aggressive group the picture is totally different. Of those patients with probably normal E.E.Gs., 39 per cent. had had head injury, while of those patients with abnormal E.E.Gs., only 19 per cent. had had head injury. The findings in the inadequate group are in accordance with one's experience that past head injury tends to produce an abnormal E.E.G. Among the aggressive group, however, one finds that head injury is less common among those with an abnormal E.E.G. than among those with a probably normal one. This suggests that the E.E.G. abnormality of aggressive persons is independent of previous head injury and that, though head injury can produce aggressiveness, and can produce dysrhythmia, these two results are probably not associated. It further suggests that dysrhythmia is commoner in the naturally aggressive psychopath than in the psychopath who is aggressive as a result of head injury.

The Influence of Epilepsy

The importance of estimating the degree to which epilepsy might increase the number of dysrhythmics among a group of aggressive psychopaths is, of course, great. Both from the clinical and from the electro-encephalographic points of view, there is plenty of evidence suggesting an association between certain forms of psychopathy and epilepsy. The episodic disturbance of behaviour, the explosive dangerousness of the aggressive psychopath who takes no thought for the consequences of his behaviour and the alleged amnesia, have led many psychiatrists to speak of an epileptoid personality. In our series, 11 patients, 8 aggressives, and 3 inadequates, had had fits in childhood which had ceased and from which they had not since suffered. The eight aggressive psychopaths had all abnormal E.E.Gs., as had two of the three inadequate cases. When fits had continued or when they were associated in time with behaviour disorder, as in 11 cases, 81 per cent. had abnormal E.E.Gs. As the figures are again small, it is impossible to claim significance, but the percentage is certainly higher than one would expect for epilepsy itself. An investigation previously made at this Unit, on about 50 psychotic epileptics, found that 69 per cent. had dysrhythmia. It is to be remembered that by far the greater number of aggressive psychopaths have never at any time had fits. Though our material includes, with large numbers of aggressive individuals only a small number of epileptics, which makes for uncertainty, yet it seems that when the two conditions occur together there is a tendency for the E.E.G. to be more frequently abnormal than when either occurs alone.

Family Histories

It has already been pointed out that Lennox, Gibbs, and Gibbs (1940) found a very high incidence of dysrhythmia among the relatives of epileptics and particularly among the parents. In this series we have classified only first-degree relatives, i.e. the parents and siblings, but it must be admitted that, as independent histories were frequently not available, the actual figures are probably not accurate. The interest and significance lie, however, in the differences within, as well as between, the two main groups. Thirty-eight per cent. of the patients of the inadequate group and 47 per cent. of the aggressive group had " positive " family histories in the widest sense in the first-degree relatives. The particular relationship which the abnormal E.E.G. has on the one hand with epilepsy and on the other with, as we have found, aggressive bad temper has led us to classify the family histories under the following headings: (1) general morbidity, which includes psychoses, psychopathic personalities, epilepsy, severe neuroses, and mental defect; (2) epileptoid states, which includes all cases of fits and bad temper; and (3) bad temper alone. Table 8 gives the percentages and the ratios between these percentages in the two groups.

TABLE 8

TYPE OF FAMILY HISTORY	AGGRESSIVES	INADEQUATES	RATIO
General morbidity	47 PER CENT.	38 PER CENT.	1·2
Epileptoid	29 ,,	15·5 ,,	1·9
Bad temper	14 ,,	5·2 ,,	2·7

In each category the aggressives show the higher incidence of abnormality. It will be seen that the ratio increases from 1·2 for general morbidity, to 1·9 for the epileptoid states generally, and to 2·7 when bad tempers alone are compared. Apart from the fact that the aggressives show a greater degree of abnormality throughout, the difference between this abnormality and that in the inadequate group becomes greatest when one narrows the investigation to the single trait —bad temper. The fact that the ratio is greatest for this trait and not for epileptoid conditions generally suggests that we are dealing with a factor which has a reality in its own right and is not merely a symptom of, say, the epileptic personality. Further, this factor is to be found among the relatives of the aggressive psychopaths nearly three times as frequently as among those of the inadequates. While none of the inadequate group admitted to suicide in the first-degree relatives, four cases were admitted by patients of the aggressive group, which suggests that aggressiveness is also to be found in the family histories of the latter. The father of another patient was confined in Broadmoor for homicide. Further evidence would probably be obtained if the investigation was extended outside the first-degree relatives. For example, one patient who was confined for homicidal attacks with alleged amnesia had a grandfather who was a murderer and later a suicide, and a paternal uncle who was also a suicide.

An examination of the E.E.Gs. of the patients whose relatives exhibit bad temper shows that while the three inadequates were negative, eight of the 13 aggressives were positive. Of the five negative cases, two were not " pure " aggressive psychopaths in the sense that one was thought to be developing a schizophrenic reaction and the other was a recidivist pilferer with aggressive crimes. Finally, there does not appear to be a greater incidence of dysrhythmia in either the aggressive or the inadequate patients whose family histories show epileptoid conditions.

Summary

Before discussing the possible explanation of the abnormal E.E.G. in psychopathic personalities, the findings may be summarized as follows. We are indebted to Dr. Eliot Slater for an examination of the results by statistical methods.

1. Forty-eight per cent. of 151 psychopathic personalities have abnormal E.E.Gs. Fifteen per cent. of 52 normal controls have abnormal E.E.Gs.

2. Sixty-five per cent. of 66 aggressive psychopaths have abnormal E.E.Gs. The more aggressive the patient the more likely is the E.E.G. to be positive. Thirty-two per cent. of 38 inadequate psychopaths have abnormal E.E.Gs.

3. Where epilepsy is associated with aggressive psychopathy, the percentage abnormal is probably much higher (82 per cent.).

4. Delinquency alone does not appear to be associated with an abnormal E.E.G.

5. Among inadequate psychopaths, head injury may account for a percentage of E.E.G. abnormality; there is no evidence that it is responsible to the same degree among aggressive psychopaths.

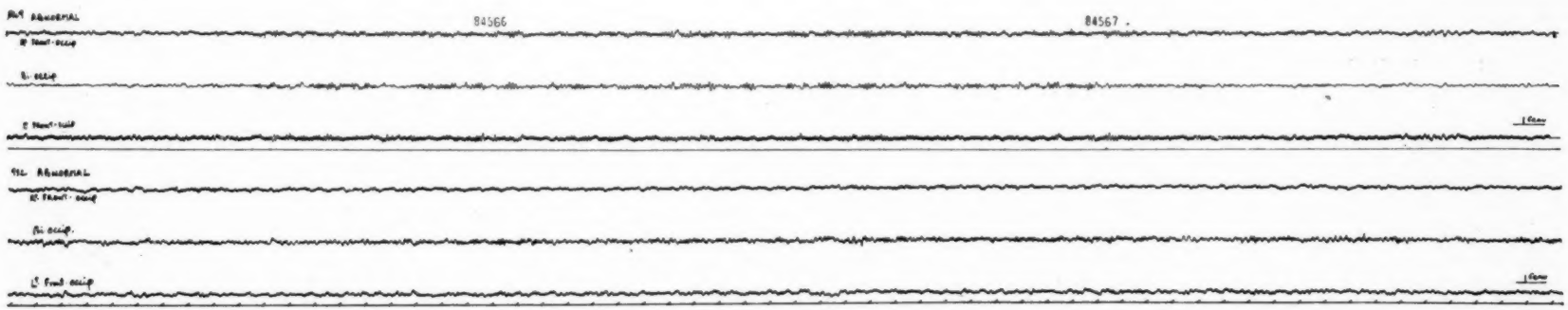
6. Examination of family histories shows that aggressive bad temper is found nearly three times as frequently among the first-degree relatives of aggressive psychopaths as among those of the inadequate group. Epilepsy is not found to the same extent. The presence of epileptoid conditions in the parents and siblings does not increase the chance of an abnormal E.E.G. in either group of patients.

Discussion

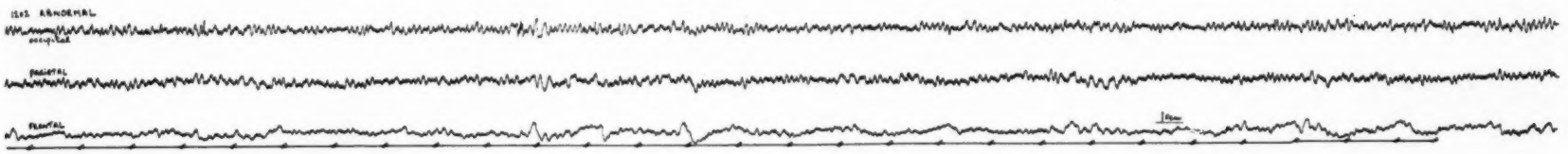
When it is remembered that no absolute knowledge as to the essential nature of cortical rhythms exists, it will be appreciated that attempts to evaluate the meaning of a generalized cortical disturbance, such as occurs, for example, in the abnormal hyperventilation response, must still be speculative. It is, we think, agreed that a localized discharge from a cortical area indicates impaired function of that area. With the exception of the hypnotic trance, there is no state of loss or true impairment of consciousness of clinically detectable degree, from any cause, that is not associated with changes in the E.E.G. There is some evidence that the spontaneous changes seen in the E.E.Gs. of epileptics are associated with changes in the *p*H of the fluid interchange through the cortical cell membrane. Nims, *et al.* (1940) have shown that the brains of petit mal epileptics have a deficient mechanism for dealing with the *p*H changes in the blood which result from the alkalosis of voluntary hyperventilation. It is typically in petit mal epileptics that the 3-cycle rhythms are produced on hyperventilation. It is therefore reasonable to ask whether the brains of aggressive psychopaths also show this defect of acid-base balance control. It is hoped, as a result of work now proceeding, to investigate this question.

Taking the E.E.G. findings alone, we must consider three factors known to influence cortical rhythms: (1) biochemical disturbances in the cerebral blood, (2) cerebral trauma either at birth or later, and (3) " constitutional defective " control of rhythms, such as Lennox, Gibbs, and Gibbs (1940) found proof of in epileptics.

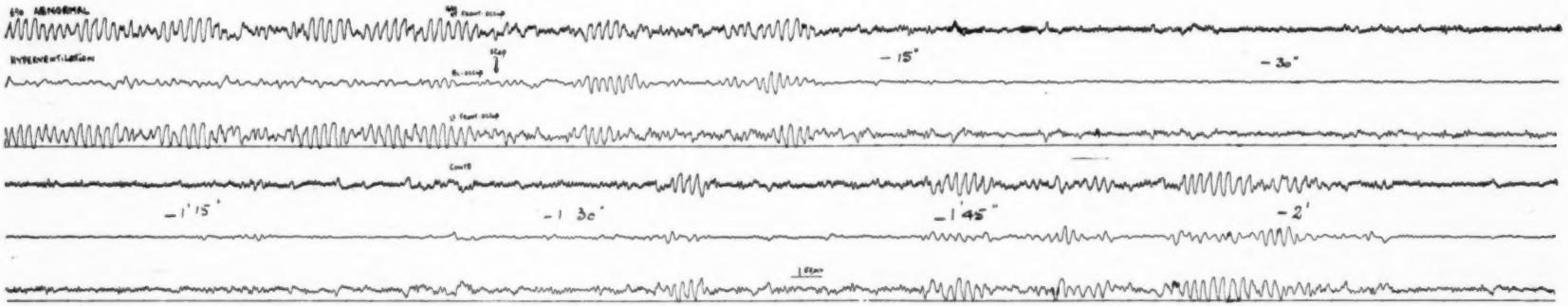
Both hypoglycæmia and oxygen lack slow cortical rhythms, but only at the stage when consciousness is impaired. Most cases of toxic encephalitis in our experience have E.E.Gs. with a preponderance of fast frequencies. The problem of excluding cerebral trauma as the cause of E.E.G. abnormality in this series is very much more difficult. None of the abnormalities found could not have been produced by trauma. We are of the opinion, however, that the tendency for the greater number of resting records to show the bilaterally synchronous abnormality, the paroxysmal quality of the discharge, and the absence of the generalized irregularity seen so frequently in chronic post-traumatic cases is against it. Further the figures in Table 6 show that, in the aggressive psychopathic group known head injury was less common among those with abnormal E.E.Gs. than among those with normal ones. This finding is surprising in view of the common experience that head injury may produce both changes in behaviour towards aggressiveness and also changes in the E.E.G. In the inadequate group, however, trauma probably accounted for a number of the 32 per cent. dysrhythmic. It can be said, therefore, that in the total group,



1. Normal 9–10 cycle dominant rhythm to the left of the record, and a burst of 3–4 cycle rhythm to the right.
2. This record characterised by the absence of a dominant rhythm within the normal frequencies. Many abnormally fast and slow frequencies.



3. This record, taken by the multi-electrode placement technique, shows the localisation of a 4-cycle focus in the parietal region.



4. This shows the abnormal response to hyperventilation. Bursts of 3 per second rhythm of high voltage occur after the cessation of hyperventilation.
5. Shows the same record one and a half minutes later, when a further burst of abnormal rhythm appears.

and particularly in the aggressive cases, there is very little positive evidence that cerebral trauma is responsible for the E.E.G. changes.

Lastly, we have the rather vague concept of constitutional defect to examine. In view of Lennox, Gibbs, and Gibbs's work (1940), this must include epilepsy. It must again be emphasized that in the present state of knowledge the E.E.G. abnormalities in this series have no specific characters. They *could* be present following trauma, in patients with epilepsy, and possibly in the immature child's cortex. As the number of epileptics examined is so few, it cannot be said that the abnormal E.E.Gs. in these cases are definitely not associated with the epileptic tendency, but only a small number of the patients have actually had fits. The figures show that it is with aggressiveness that the E.E.G. shows the consistent abnormality. The more aggressive the patient, the more likely is the E.E.G. to be abnormal. In the relatives of aggressive persons, bad temper is found more frequently than epilepsy. It would be valuable to examine the E.E.Gs. of the relatives of aggressive persons. Apart from the psychoanalytical interpretation of inadequate psychopathy there is nothing to suggest that the latter contains an element of aggressive behaviour, nor with such cases would one associate the epileptic tendency, and yet this group had twice as many abnormal E.E.Gs. as the controls.

✓ The idea of a cortical immaturity, with failure to reach adult control of rhythms, is in our opinion, worthy of consideration. The work of Jasper, Solomon, and Bradley (1938) emphasizes the association between bad-tempered, irritable children and abnormal E.E.Gs. Brill and Seidemann (1941), in a careful study of the E.E.Gs. of 100 normal children, show that the alpha frequency increases, and the incidence of slow activity diminishes with advancing age, the critical level for normality being reached at the age of nine and a half, though the frequency may go on increasing until 15. They also demonstrate a marked tendency for the abnormal hyperventilation response to appear in the E.E.Gs. of normal children, and state that this has no significance in childhood. In view of the similarity between the aggressive behaviour of psychopaths and the normal bad-temper response to frustration in young children on the one hand, and the similarity between the E.E.Gs. of aggressive psychopaths and those of young children on the other, the suggestion that the abnormality in the E.E.Gs. in these cases is produced by a failure of development in the central nervous system is very tempting. It fits in with our psychiatric, biological, and social conceptions of psychopathic personalities. Combining the data obtained in this investigation with those recently published by Williams (1941a), who used similar apparatus and criteria, we may construct the following table of ascending groups of abnormality.

TABLE 9

CATEGORY	ABNORMAL
Highly selected flying personnel (successfully completed training)	5 per cent. (Williams)
R.A.M.C. personnel	10 per cent. (Williams)
Mixed controls	15 per cent. (Hill & Watterson
Mixed psychoneurotics	26 per cent. (Williams)
Inadequate psychopaths	32 per cent. (Hill & Watterson)
Aggressive psychopaths	65 per cent. (Hill & Watterson)

Examination of our own control group has led us to agree with Williams' statement that " the incidence of abnormality in a perfectly normal group of subjects may be halved by further selection upon criteria having no apparent relationship to electro-encephalographic selection." In our cases the criteria proved to be aggressiveness and irritability. On the evidence gathered by us from control material and patients, and on that obtained by other workers, one can have little doubt that an abnormal E.E.G. constitutes for its possessor a handicap in the business of biological adaptation, failure of which may show itself, as in our present series, in undesirable, asocial behaviour.

We are indebted to the medical officers of the neuro-psychiatric unit and of the military mental hospital for referring cases to us; to Dr. Eliot Slater, Clinical Director of the neuro-psychiatric unit, for helpful criticism and advice, especially regarding statistical data; to Mr. J. Theobalds, electro-encephalographic technical assistant at this unit; and to Colonel A. A. W. Petrie and to Dr. Louis Minski for permission to publish the case material.

REFERENCES

Berger, H. (1936). *Arch. Psychiat. Nervenk.*, **104,** 678.
Brill, N. Q., and Seidemann, H. (1941). *Amer. J. Psychiat.*, **98,** 250.
Cohen, L. H. (1938). *J. ment. Sci.*, **84,** 284.
Gibbs, F. A., and Gibbs, E. L. (1941). *Atlas of Electro-encephalography.* (Mass.)
Golla, F., Graham, S., and Walter, W. G. (1937). *J. ment. Sci.*, **83,** 137.
Gottlober, A. B. (1938*a*). *J. exp. Psychol.*, **22,** 67.
Grass, A. M., Gibbs, F. A. (1938). *J. Neurophysiol.*, **1,** 521.
Henderson, D. K. (1939). *Psychopathic States.* Chapman & Hall, London.
Hoagland, H., Cameron, D. E., and Rubin, M. A. (1937). *Amer. J. Psychiat.*, **94,** 183.
Jasper, H. H., and Kerschman, J. (1941). *Arch. Neurol.* Paris, **45,** 903.
Jasper, H. H., Kerschman, J., and Elvidge, A. (1940). *Arch. Neurol. Psychiat.* (Chicago), **44,** 328.
Jasper, H. H., Solomon, P., and Bradley, C. (1938). *Amer. J. Psychiat.*, **95,** 641.
Kahn, E. (1931). *Psychopathic Personalities.* Yale University Press, New Haven.
Lemere, F. (1936). *Brain*, **59,** 366.
Lennox, W. G., Gibbs, E. L., and Gibbs, F. A. (1940). *Arch. Neurol. Psychiat.* (Chicago), **44,** 1,155.
Lindsley, D. B., and Cutts, K. K. (1940). *Ibid.*, **44,** 1,199.
Menninger, K. A. (1938). *Man Against Himself.* Harrap, London.
MacMahon, J. F., and Walter, W. G. (1938). *J. ment. Sci.*, **84,** 781.
Nims, L. F., Gibbs, E. L., Lennox, W. G., Gibbs, F. A., and Williams, D. (1940). *Arch. Neurol. Psychiat.* (Chicago), **43,** 262.
Putnam, T. J., and Merritt, H. H. (1941). *Arch. Neurol. Psychiat.* (Chicago), **45.** 797.
Rubin, M. A., and Cohen, L. H. (1939). *J. ment. Sci.*, **85,** 779.
Saul, J. L., Davis, H., and Davis, P. A. (1937). *Traus. Amer. neurol. Ass.*, **63,** 167.
—— (1937). *Proc. Roy. Soc. Med.*, **30,** 33.
Walter, W. G. (1942). *J. ment. Sci.*, **88,** 370, 110.
Williams, D. (1941*a*). *J. Neurol. Psychiat.*, **4** (new series), 257.
—— (1941*b*). *J. Neurol. Psychiat.*, **4,** 131.

EPITOME OF CURRENT JOURNALS

AMERICAN JOURNAL OF PSYCHIATRY

Vol. 98. No. 3. November 1941.

The Military Psychiatrist at Work. W. C. Porter. 317.
The Clinical Differentiation of Senile and Arteriosclerotic Psychoses. D. Rothschild. 324.
Narcolepsy. W. F. Murphy. 334.
Encephalopathia Alcoholica. N. Joliffe and H. Wortis. 340.
The Incidence and Significance of Alcoholism in the History of Criminals. M. G. Gray and M. Moore. 347.
Brain Metabolism, VIII. The Effects of Electric Shock and Some Newer Drugs. S. B. Wortis, D. Shaskan, D. Impastato, and R. Almansi. 354.
Prognostic Criteria in Schizophrenia. L. S. Chase and S. Silverman. 360.
Insulin Convulsions. A Method of Prevention. J. P. Frostig, C. R. Bennett, J. Schreiber, and G. F. Thomas. 369.
Encephalography in Schizophrenia. K. H. Finley and C. M. Campbell. 374.
Follow-Up Results in Insulin Shock Therapy after One to Three Years. T. D. Rivers and E. D. Bond. 382.
Electroencephalographic Studies of Corticohypothalamic Relations in Schizophrenia. R. B. Grinker and H. M. Serola. 385.
The Vitamin B_1 Requirement during Insulin Shock Therapy. W. Goldfarb and K. M. Bowman. 393.
The Treatment of Childhood Schizophrenia by Metrazol Shock Modified by B-Erythoidin. F. Cottington. 397.
The Effect of Convulsive Treatment on Memory. I. Sherman, J. Mergener, and D. Levitin. 401.
Electroencephalographic Studies in Organic Psychoses. P. Hoch and J. Kubis. 404.
Studies on the Corpus Callosum, VIII. The Effects of Partial and Complete Section of the Corpus Callosum of Psychopathic Epileptics. A. J. E. Akelaitis. 409.
Experiences with a New Criminal Code in New York State. B. Apfelberg. 415.
Parallel Psychological, Psychiatric, and Physiological Findings in Schizophrenic Patients under Insulin Shock Treatment. B. H. McNeel, J. G. Dewan, C. R. Myers, L. D. Proctor, and J. E. Goodwin. 422.
Electroencephalograms of Manic-Depressive Patients. P. A. Davis. 430.
Evaluation of the Results of Psychoanalytic Therapy R. P. Knight. 434.
Mental Disorder in One of a Pair of Identical Twins. G. E. Hobbs. 447.
Psychiatric Observations on Children with Abdominal Pain. J. P. Lambert. 451.
Ordinal Position and Schizophrenia. R. M. Patterson and T. W. Zeigler. 455.
Disorganizing Factors of Infant Personality. M. A. Ribble. 459.

ARCHIVES OF NEUROLOGY AND PSYCHIATRY, CHICAGO

Vol. 46. No. 3. September 1942.

*Objective Measurement of Relative Intracranial Blood Flow in Man, with Observations concerning the Hydrodynamics of the Craniovertebral System. E. B. Ferris. 377.
*Corpus Striatum and Thalamus of a Partially Decorticate Monkey. S. W. Ranson, S. W. Ranson, Junr., and M. Ranson. 402.
*Subcortical Hematoma: Surgical Treatment, with Report of Eight Cases. C. Pilcher. 416.
*Hepatolenticular Degeneration: Report of a Case. C. G. Babcock and H. W. Brosin. 431.
Multiple Meningioma: Removal of Ten Intracranial Tumors from a Patient. D. H. Echols. 440.
Vascular Malformations and Vascular Tumors involving the Spinal Cord: A Pathologic Study of Forty-Six Cases. O. A. Turner and J. W. Kernohan. 444.
*Peripheral Neuropathy: Evaluation of Sensory Findings. M. H. Stein, H. Wortis, and N. Joliffe. 464.
*Tabes Dorsalis: Evaluation of the Sensory Findings. M. H. Stein and H. Wortis. 471.
*Changes in the Brain in Pertussis with Convulsions. V. B. Dolgopol. 477.
*Observations on Monkeys with Bilateral Lesions of the Globus Pallidus. S. W. Ranson and C. Berry. 504.
*Intracranial Blood Flow in Insulin Coma. E. B. Ferris, M. Rosenbaum, C. D. Aring, H. W. Ryder, E. Roseman, and J. R. Hawkins. 509.

Objective Measurement of Intracranial Blood Flow.—For the objective measurement of a function of total intracranial blood flow in man, a method was devised which in its basic principle resembled that used to study the blood flow to extremities by the venous occlusion plethysmographic method. The values obtained appear to be of the same order of magnitude as the actual volume flow of blood through the cranium. It is estimated that the total intracranial blood flow of normal man does not exceed levels of 250 to 400 c.c. per minute under the conditions of these experiments. (R.M.S.)

Corpus Striatum and Thalamus.—A study of the fibre connections of the corpus striatum and thalamus of a partially decorticate monkey. (R. M. S.)

Subcortical Hæmatoma.—Eight cases of solitary subcortical hæmatoma, in all of which the patients were subjected to surgical therapy, are reported. In three cases hæmorrhage was of traumatic origin, in four it was spontaneous, and in the eighth the case was doubtful. The ages of the patients varied from 5 to 62 years, but six patients were under 40. In six cases the

location was temporal or parietal, in one frontal and in one cerebellar. There were no operative deaths, but two of the patients died six and nine months later, respectively: one of pneumonia and one of unknown cause. The symptomatology, diagnosis, pathology, operative treatment, and surgical results are discussed. (R. M. S.)

Hepatolenticular Degeneration.—A case of hepatolenticular degeneration is described with emphasis on the mental status of the patient, and the absence of tremor at the time the diagnosis was made. With the usual methods of testing hepatic function (van den Bergh, bilirubin excretion and bromsulphalein tests), no abnormality was found, but the patient was found to have prothrombin deficiency, a condition which may be interpreted as indicative of hepatic damage. (R. M. S.)

Peripheral Neuropathy.—Sensory dissociation is a characteristic feature of the peripheral neuropathy complicating alcoholism and other conditions associated with disturbed nutrition. Light touch, vibration, and position senses and " first " pain sense are affected earliest and most severely. These sensations are carried by the large, myelinated A and B fibres, which are affected earliest and most severely in such conditions. " Second " pain sense, which is conveyed along the slow, unmyelinated C fibres, is spared. Immediate dysesthesia represents a stage of injury of the peripheral nerve at which some of the myelinated (A and B) fibres are still functioning, while others have been blocked. Delayed dysesthesia represents the stage at which practically all of the myelinated (A and B) fibres have been blocked, only small, unmyelinated fibres continuing to function. The delay in perception results from the very slow transmission along the C fibres. The sensory dissociation and dysesthesia of peripheral neuropathy may be duplicated experimentally by producing ischemia of an extremity. As the ischemia progresses, the loss of function of the peripheral nerve becomes more severe and the dysesthesia changes from the immediate to the delayed type. In peripheral neuropathy of this type, the large, myelinated (A and B) fibres are primarily affected. This indicates that these fibres have greater metabolic needs, and are therefore most susceptible to nutritional deficiency. (R. M. S.)

Tabes Dorsalis.—Sensory dissociation and dysesthesia were noted in 18 patients with tabes dorsalis. In 11 of these patients the dysesthesia was delayed, and in each of these there was marked delay in pain perception. The delay in pain perception and the dysesthesia have been related to blocking of fast conducting impulses, allowing more slowly conducted impulses to be perceived at a later time and in uninhibited fashion. It is suggested that the physiological mechanism of the delayed pain perception and dysesthesia associated with tabes dorsalis is analogous to that previously noted with disorders of the peripheral nerve. (R. M. S.)

Brain Changes in Pertussis.—The changes in the brain in pertussis are apparently noninfectious. They are most likely of circulatory origin and consist in œdema, ischemic cellular degeneration, multiple hæmorrhages (usually small) and lymphocytic plugs in veins and capillaries. On rare occasions a secondary " Encephalitic reaction " may be observed in addition to the aforementioned changes. (R. M. S.)

Bilateral Lesions of Globus Pallidus.—Three monkeys with large bilateral lesions in the globus pallidus showed none of the signs which point to striatal disease in man. None of the animals showed cogwheel resistance to passive movement; none had any trace of a Parkinsonian tremor. Choreiform and athetoid movements did not occur. The animals did not have the typical mask-like face and slowness of movement characteristic of paralysis agitans. The question is raised whether damage to the hypothalamus may not play a part in producing the Parkinsonian syndrome in man. (R. M. S.)

Intracranial Blood Flow in Insulin Coma.—The authors conclude from their studies that hypoglycemia coma, induced by the administration of insulin, is associated with either no change or a slight increase in total intracranial blood flow. (R. M. S.)

Vol. 46. No. 4. October 1941.

*The Wernicke Syndrome. N. Joliffe, H. Wortis, and H. D. Fein. 569.
The Electroencephalogram as an Aid in the Study of Narcolepsy. J. B. Dynes and K. H. Finley. 598.
*The Cortical Frequency Spectrum in Epilepsy. F. A. Gibbs, W. G. Lennox, and E. L. Gibbs. 613.
*Cutaneous Pressure-Vibration Spots and their Underlying Tissues. B. v. H. Gilmer and S. R. Haythorn. 621.
*Effect of Nicotinic Acid and Related Substances on the Intracranial Blood Flow of Man. C. D. Aring, H. W. Ryder, E. Roseman, M. Rosenbaum, and E. B. Ferris. 649.
*Muscular Shortening and Dystrophy. A Heredofamilial Disease. A. Hauptmann and S. J. Thannhauser. 654.
*Characteristics of After-Discharge following Cortical Stimulation in the Monkey. M. R. Sapirstein. 665.
*Anticonvulsive Action of Azosulamide in Patients with Epilepsy. M. H. Cohen and S. Cobb. 676.
Physiology of the Spinal Cord: I. Role of the Anterior Column in Hyperreflexia. O. R. Hyndman. 695.
*Cerebral Arteriography: Its Place in Neurologic Diagnosis. S. W. Gross. 704.

Wernicke Syndrome.—Twenty-seven cases of Wernicke's syndrome (three of which occurred in non-alcoholic patients) are analysed and the following conclusions

reached. The syndrome as originally described by Wernicke is probably a combination of several nutritional deficiencies affecting the nervous system and need not necessarily be complete in any case. The authors' results indicate that (a) the ophthalmoplegia is a thiamine deficiency; (b) the clouding of consciousness may be related to anything which interferes with proper cerebral metabolism, some of the known offenders being lack of carbohydrate, lack of oxygen, lack of thiamine or nicotinic acid or riboflavin or of all three, and probably a lack of many other substances now under investigation; and (c) the ataxia is difficult to evaluate and its response to therapy has not as yet been worked out. Other deficiency syndromes may and do superimpose themselves on the more usual Wernicke picture, and these require specific treatment. The ophthalmoplegia is invariably preceded or accompanied by peripheral neuropathy. Delirium, with its marked increase in psychomotor activity, and hence in total metabolism, frequently precedes the development of this syndrome. In the recovered patients, the development of a Korsakoff syndrome is the rule. This does not show a consistent response to thiamine hydrochloride, as has frequently been claimed. (R. M. S.)

Cortical Frequency Spectrum in Epilepsy.—The Grass method of frequency analysis has been used to obtain the cortical frequency spectrums of epileptic patients, of the parents of epileptic patients, and of normal persons. Study of records made during seizures discloses the following: (a) In petit mal attacks a disproportionately high peak appears in the 2 to 3 per second region; (b) in a psychomotor seizure an abnormally high peak appears in the 4 to 7 per second region; and (c) in grand mal attacks an abnormally high peak is evident in the 20 to 29 per second region. The average spectrums of epileptic patients made in the intervals between seizures disclose a disproportionately large amount of energy at frequencies below 9 per second. However, the subgroup of patients subject only to grand mal have an abnormally great amount of energy in the 20 to 29 per second region. Patients having periodic grand mal attacks show an increase in energy in the faster frequencies as the day or the hour of the convulsion approaches. The average spectrums of a group of parents of epileptic patients show abnormalities similar to those seen in the average spectrums of epileptic patients, but these abnormalities are less extreme. (R. M. S.)

Cutaneous Pressure-Vibration Spots.—Excision studies failed to substantiate the conventional claim that the cutaneous pressure qualities are mediated by specific sense receptors, since the sites for study were selected with extreme care and no such receptors were found. The possibility that the neurovascular system of the skin operates either in a direct or in an indirect manner in the mediation of cutaneous pressure and vibration is suggested by two observations. (a) The neurovascular system of the skin contains certain structural units richly endowed with a nerve supply, surrounded by regions of less nerve concentration. (b) Biopsy specimens taken from the cutaneous areas highly sensitive to pressure and vibratory stimulation were found to contain a richer afferent arterial nerve supply than the specimens taken as controls in which the tissue was less sensitive to pressure and vibration. The presence in several of the biopsy specimens from spots sensitive to pressure and vibration of certain tubular, straight canals having muscular walls which appeared to unite the glomus bodies of the stratum subcutaneum with the capillary zone of the stratum papillare and the presence of its rich reticular nerve supply served to strengthen the authors' belief that the arteriovenous anastomoses in the skin are in some way related to sensory interpretations. (R. M. S.)

Nicotinic Acid and Intracranial Blood Flow.—Nicotinic acid and quinine nicotinate administered intravenously increase the intracranial blood flow for periods lasting from 20 to 60 minutes. This effect, which parallels the flushing of the skin, diminishes gradually after the height of the reaction, which occurs within several minutes of the injection. Nicotinic acid amide has no significant effect on the total intracranial blood flow; neither does it cause flushing of the skin. (R. M. S.)

Muscular Shortening and Dystrophy.—A hereditary familial disease has been described. It is characterized by a short, "webbed" neck as well as by shortness of the neck muscles, long dorsal muscles, and flexor muscles of the upper portions of the arms. This shortness prevents the complete bending of the neck and back, as well as the stretching of the arms. There are also underdevelopment and weakness of the proximal muscles of the arms and the gluteal muscles. Decrease in or absence of deep reflexes was found in some members of the family. The webbing, which is formed by the shortened trapezius muscle, causes the neck to appear broader than usual. The cervical portion of the spinal column was normal. Roentgen examination revealed that all the vertebræ were present. The outstanding symptom of this disease is the shortening of certain muscles. In some cases, some features of progressive muscular dystrophy were present. However, most of the members of this family exhibited mainly shortening and underdevelopment of some muscles. The authors, therefore, believe that this heredofamilial anomaly is a special type of heredofamilial muscular disease. (R. M. S.)

After-Discharge following Cortical Stimu-

lation.—A report of a study of tonic and clonic after-discharges following cortical stimulation in monkeys, both before and after cortical and subcortical ablations. (R. M. S.)

Anticonvulsive Action of Azosulfamide.—The red dye azosulfamide is shown to have anticonvulsive action in some patients with epilepsy. No serious toxic effects were encountered. (R. M. S.)

Cerebral Arteriography.—Cerebral arteriography is indicated for the detection and localization of intracranial aneurysms, especially in recurring attacks of "spontaneous" subarachnoid hæmorrhage. It is also indicated for the localization of intracranial arteriovenous fistulas, varices, vascular tumours and vascular malformations, for the differentiation of aneurysm and tumour and for the localization of neoplasms when the result of pneumoencephalographic examination is not conclusive. (R. M. S.)

Vol. 46. No. 5. November 1941.

*Vascular Supply of the Spinal Ganglia. L. Bergmann and L. Alexander. 761.
*Pathology of Amyotrophic Lateral Sclerosis: Fiber Analysis of the Ventral Roots and Pyrimidal Tracts of the Spinal Cord. G. Wohlfart and R. L. Swank. 783.
*Studies in Diseases of Muscle: X. Prostigmine and Physostigmine in the Treatment of Myasthenia Gravis. A. T. Milorhat, with the technical assistance of W. E. Bartels. 800.
*Neurologic Symptoms following Extensive Occlusion of the Common or Internal Carotid Artery. A. B. King and O. R. Langworthy. 835.
*A New Method for Treatment of Cystic Craniopharyngioma by Intraventricular Drainage. J. E. Scarff. 843.
*Roentgenologic Changes in the Bones in Cases of Pseudohypertrophic Muscular Dystrophy. B. S. Epstein and J. L. Abramson. 868.
*Topical Arrangement within the Spinothalamic Tract of the Monkey. T. A. Weaver and A. E. Walker. 877.
Metrazol Convulsions in the Treatment of the Psychosis of Dementia Paralytica. V. B. Kenyon, M. Lozoff, and D. Rapaport. 884.
Dilatin Hyperplastic Gingivitis: Its Treatment and Prevention. D. E. Ziskin, L. R. Stowe, and E. V. Zegarelli. 897.
*Removal of Tumor Arising Anterior to the Medulla. A. Ecker. 908.

Vascular Supply of Spinal Ganglia.—Most of the vessels supplying the spinal ganglion originate from the main vascular trunk (the spinal arterial branch) at right angles or by way of recurving arcs, arising off and frequently against the direction of the blood flow in the mother branch. This explains the fact that higher pressure and a longer time are needed to inject the arteries of the spinal ganglion than the spinal and radicular ramifications of the same segmental vessel. If analogy drawn from other, better known parts of the nervous system is permissible, the arterial supply of the spinal ganglia may be considered to be rather vulnerable. There may be some relation between this fact and the frequent occurrence of cellular loss in the spinal ganglia, reduction in the number of posterior root fibres and mild degeneration of the posterior column in an otherwise normal spinal cord after the third decade of life, a concept which is further substantiated by the gradual reduction of sensibility, most readily discernible as a reduction of vibratory sense, from the third decade of life on. (R. M. S.)

Pathology of Amyotrophic Lateral Sclerosis.—In five cases of amyotrophic lateral sclerosis measurements showed that most of the large nerve fibres in the ventral spinal roots had disappeared, whereas the small fibres appeared normal. The large ventral horn nerve cells suffered a similar fate, the small cells remaining relatively normal. Accurate measurements of the corticospinal tract fibres were made impossible by glial tissue, but it appeared that here the large fibres also suffered the greater damage. All posterior spinal roots appeared normal. In two cases in which bilateral degeneration of the pyramidal tracts was marked muscular hypertonus was not noted, the deep reflexes were normal or hypoactive and extensor plantar responses were absent. In these cases the large fibres in the ventral roots were more extensively damaged than in any of the other cases. It might be inferred from this observation that signs of degeneration of the pyramidal tracts are dependent for their production on the large ventral root fibres. (R. M. S.)

Diseases of Muscle.—A valuable contribution to the study of the effects of prostigmine with a discussion of the factors limiting the use of this drug in the treatment of myasthenia gravis. (R. M. S.)

Neurologic Symptoms following Occlusion of Internal Carotid Artery.—Occlusion of the carotid artery produces atrophy of the optic nerve and loss of vision in the eye on the same side, due to closure of the ophthalmic artery. The circulation is also impaired in the anterior choroidal, anterior cerebral and middle cerebral arteries, which are terminal branches of the internal carotid artery. There may occur softening of the brain, which is usually maximal in the field of the middle cerebral artery. Temporal hemianopia, due to involvement of the optic radiation, may be present in the visual field of the opposite eye. Contralateral hemiplegia and hemianesthesia, more marked in the face and arm than in the leg, also result; they appear to be due to cortical destruction rather than to injury to the internal capsule. If the left cortex is involved in a right-handed person, there may be a variable degree of aphasia. Dysarthria and dysphagia are often present during the first few days after the vascular occlusion, but disappear later. (R. M. S.)

Treatment of Cystic Craniopharyngioma by Intra-Ventricular Drainage.—A new

method of treating craniobuccal cysts, characterized as intra-ventricular drainage, is here described. The basic principle consists of establishing a communication between the dome of the cyst and the floor of the lateral ventricle. (R. M. S.)

Bony Changes in Pseudohypertrophic Muscular Dystrophy.—The older view that muscular dystrophy is a disease which involves muscle only may have to be revised to include the concept of a more generalized pathological process. In addition to the alterations in creatinine and carbohydrate metabolism and the possible disturbance of the endocrine glands, there is involvement of bone, as indicated by the authors' roentgenographic studies. It is the authors' opinion that the changes cannot be explained on the basis of disuse alone, but may be an expression of a mesodermal defect, resulting in muscular and skeletal defects. (R. M. S.)

Topical Arrangement within Spinothalamic Tract.—The course and localization of the spinothalamic tract were traced in 11 monkeys after anterolateral chordotomies and midline posteroanterior myelotomies had been performed at different levels of the spinal cord. In general, as higher levels in the spinal cord are reached, fibres from lower segments tend to become concentrated laterally and dorsally within the anterolateral column, and fibres from higher level s are situated more medially and inferiorly although there is no absolute segregation at any level. Within the medulla, fibres from the lower levels are concentrated at the periphery of the bulb, whereas fibres from the cervical region lie medially. Although there is evidence that such an arrangement exists, the topical localization of the fibres in the pons, the midbrain or within the nucleus ventralis posterior of the thalamus could not be demonstrated by the methods used in this investigation. (R. M. S.)

Removal of Tumour arising Anterior to Medulla.—There is reported a second case of apparently complete, successful removal of a meningioma which arose from the anterior rim of the foramen magnum and which had displaced the medulla and spinal cord backward. (R. M. S.)

BRAIN

Vol. 64. No. 4. December 1941.

Phantom Limbs and Body Shape. G. Riddoch. 197.
Cerebral Electrical Changes in Experimental Concussion. D. Williams and D. Denny-Brown. 223.
The Component Reflexes of Micturition in the Cat. Part III. F. J. F. Barrington. 239.
Visual Disorientation with Special Reference to Lesions of the Right Cerebral Hemisphere. W. R. Brain. 244.
Akinetic Mutism with an Epidermoid Cyst of the 3rd Ventricle. H. Cairns, R. C. Oldfield, J. B. Pennybacker, and D. Whitteridge. 273.
A Note on the Clinical Anatomy of the Veins ,with Special Reference to the Spinal Veins. H. A. Harris. 291.

Vol. 6. No. 1. March 1942.

*Structure of the Neurohypophysis with Special Reference to Nerve Endings. E. Vazquez-Lopez. 1.
*The Systemic Nervous Affinity of Triorthocresyl Phosphate (Jamaica Ginger Palsy). C. D. Aring. 34.
*The Anatomy and Physiology of Cutaneous Sensibility: A Critical Review. F. M. R. Walshe. 48.

Neurohypophysis and Nerve Endings.—Histological examination of the pars nervosa of the horse pituitary has been made after silver or gold impregnation. In contrast to previous work the whole structure has been studied as a functional entity, fibrous tissue, blood vessels, neuroglia, nerve fibres and all bodies being examined in relation to each other, with a view to assessing their function. It seemed that the very large number of nerve endings of sensory pattern were so arranged that they formed a perivascular receptive apparatus. This lead to the conclusion that the nerves of the pars nervosa are mainly centripetal conductors, and that the pars nervosa is primarily a sensory organ. There was no evidence that it is a specific gland of internal secretion, but rather it constitutes a chemo-receptive or presso-receptive apparatus devoted to the reception of stimuli which enable the hypothalamic centres to control the metabolic and hormonal functions of the body by detecting variations in the composition and pressure of the blood. (D. W.)

Systemic Nervous Affinity of Triorthocresyl Phosphate.—The condition begins as a severe polyneuritis with involvement, especially of motor function 7 to 14 days after ingestion of the poison. The lesions were seen in the nerves, the anterior horn cells of the cord and in one case in the motor cells of the medulla. The late results of the disorder, and observations of three recent cases showed that extensive degenerative changes occurred in the cord, notably in the pyramidal tract. Histological examination in 36 patients showed widespread change in muscles, blood vessels, peripheral nerves, cord and also in the brain stem and cerebral hemispheres. The clinical end result and the parenchymatous changes resembled amyotrophic lateral sclerosis. The peripheral changes in nerves and muscles may have been secondary to vascular damage, but the

evidences that the central parenchymal changes were secondary are less convincing. (D. W.)

Cutaneous Sensibility.—This review includes a full statement and critical analysis of the clinical experimental observations, with sections on Head and Rivers' theory of the afferent nervous system, Trotter and Davies' observations in cutaneous sensibility, and Borings' experiment on nerve division. It then deals with the electrophysiological study of sensory function and the anatomy of cutaneous sensibility. The problems of cutaneous pain and tactile sensibility and of the validity of Lewis's hypothesis of a nocifensor mechanism are dealt with in the light of present anatomical knowledge. (D. W.)

JOURNAL OF CLINICAL INVESTIGATION

Vol. 20. No. 6. November 1941.

The Cause of Death in Experimental Anuria. H. E. Hoff, P. K. Smith, and A. W. Winkler. 607.

The Thiamin Content of Human Blood and Urine as determined by the Fermentation Method. R. Goodhart. 625.

Note on the Interpretation of Clearance Methods in the Diseased Kidney. H. W. Smith. 631.

Effective Renal Blood Flow in Subjects with Essential Hypertension. H. Chasis and J. Redish. 655.

An Epidemic of Influenza. Results of Prophylactic Inoculation of a Complex Influenza A—Distemper Vaccine. J. W. Brown, M. D. Eaton, G. Meiklejohn, J. B. Lagen, and W. J. Kerr. 663.

Circulatory Failure in Acute Infections. R. V. Ebert, and E. A. Stead. 671.

Studies on Intrapulmonary Mixture of Gases. IV. The Significance of the Pulmonary Emptying Rate and a Simplified Open Circuit Measurement of Residual Air. A. Cournand, E. De F. Baldwin, R. C. Darling, and D. W. Richards. 681.

A Comparison between Dehydration from Salt Loss and from Water Deprivation. J. W. Nadal, S. Pedersen, and W. G. Maddock. 691.

Calculation of the Venous-Arterial Shunt in Congenital Heart Disease. M. Prinzmetal. 705.

The Plasma Levels of Vitamin A after the Ingestion of Standard Doses: Studies in Normal Subjects and Patients with Cirrhosis of the Liver. E. P. Ralli, E. Bauman, and L. B. Roberts. 709.

The Hemodynamic Effects of Angiotonin in Normal Man. S. E. Bradley and B. Parker. 715.

The Nature of the Arterial Hypertension produced in Normal Subjects by the Administration of Angiotonin. R. A. Wilkins and C. N. Duncan. 721.

Some Properties of Human Fetal and Maternal Blood. R. C. Darling, C. A. Smith, E. Asmussen, and F. M. Cohen. 739.

Metabolic Studies in Patients with Cancer of the Gastro-Intestinal Tract. I. Plasma Vitamin A Levels in Patients with Malignant Neoplastic Disease, particularly of the Gastro-Intestinal Tract. J. C. Abels, A. T. Gorham, G. T. Pack, and C. P. Rhoads. 749.

Fractionation of Serum Proteins in Hyperproteinemia, with Special Reference to Multiple Myeloma. A. B. Gutman, D. H. Moore, E. B. Gutman, V. McClellan, and E. A. Kabat. 865.

Vol. 21. No. 1. January 1942.

The Cardio-circulatory Effects in Man of Neosynephrin (l-*a*-hydroxy-*β*-methylamino-3-hydroxyethylbenzene hydrochloride). A. Keys and A. Violante. 1.

The Cardio-circulatory Effects in Man of Synephrin Tartrate (dl-*a*-hydroxy-*β*-methylamino-4-hydroxyethylbenzene hydrochloride). A. Keys and A. Violante. 13.

The Changes in the Blood Pressure and in the Renal Blood Flow and Glomerular Filtration Rate of Hypertensive Patients following Unilateral Nephrectomy. M. Friedman, A. Selzer, H. Kreutzmann, and J. J. Sampson. 19.

Radioactive Iodine as an Indicator in Thyroid Physiology: IV. The Metabolism of Iodine in Graves' Disease. S. Hertz, A. Roberts, and W. T. Salter. 25.

Radioactive Iodine as an Indicator in Thyroid Physiology: V. The Use of Radioactive Iodine in the Differential Diagnosis of Two Types of Graves' Disease. S. Hertz and A. Roberts. 31.

The Rôle of the Adrenal Cortex in Acute Anoxia. R. A. Lewis, G. W. Thorn, G. F. Koepf, and S. S. Dorrance. 33.

Effects of Interrupting and Restoring the Circulation to the Lower Extremities. D. Dauber, M. Landowne, L. N. Katz, and H. Weinberg. 47.

The Filtration Rate, Effective Renal Blood Flow, Tubular Excretory Mass and Phenol Red Clearance in Normal Pregnancy. C. A. Welsh, I. Wellen, and H. C. Taylor, Jr. 57.

The Filtration Rate, Effective Renal Blood Flow, Tubular Excretory Mass and Phenol Red Clearance in Specific Toxemia of Pregnancy. I. Wellen, C. A. Welsh, and H. C. Taylor, Jr. 63.

*The Prevention of Sensory Neuron Degeneration in the Pig, with Special Reference to the Rôle of Various Liver Fractions. M. M. Wintrobe, C. Mufiatt, J. L. Miller, Jr., L. C. Kolb, H. J. Stein, and H. Lisco. 71.

*Pathological Variations in Blood and Spinal Fluid Pyruvic Acid. E. Bueding, H. Wortis, and M. Stern. 85.

The Significance of Porphynuria in Lead Poisoning. R. Kark and A. P. Meiklejohn. 91.

The Acid-Base Balance of Premature Infants. W. S. Branning. 101.

Renal Function in Patients with Addison's Disease and in Patients with Adrenal Insufficiency Secondary to Pituitary Pan-hypofunction. J. H. Talbott, L. J. Pecora, R. S. Melville, and W. V. Consolazio. 107.

Sensory Neuron Degeneration.—Abnormal gait and sensory neuron degenerative changes in pigs produced by factors deficient in the diet other than thiamin, riboflavin and nicotinic acid were prevented when dessicated whole liver or brewer's yeast were fed. The various fractions obtained in manufacture of anti-pernicious anæmia extract were also tested for protection, and that used in the treatment of pernicious anæmia was most effective when given orally in large doses. (J. N. C.)

Variations in Blood and Spinal Fluid Pyruvic Acid.—Fasting pyruvic acid levels in blood and c.s.f. were examined and variation from the normal was found in "acute" peripheral neuropathy and in most of the cases associated with hyperpyrexia. (J. N. C.)

Vol. 21. No. 2. March 1942.

Studies on the Influence of Vitamin A and Vitamin C on Certain Immunological Reactions in Man. A. E. Feller, L. B. Roberts, E. P. Ralli, and T. Francis, Jr. 121.
The Influence of Diet on the Ascorbic Acid Requirement of Premature Infants. M. Dann. 139.
Bleeding Time, Lymph Time, and Clot Resistance in Men. A. L. Copley and J. J. Lalich. 145.
The Significance of the D:N Ratio and its Bearing on the Mechanism of Diabetes Mellitus. D. R. Drury. 153.
The Measurement and Metabolism of Thiamin and of a Pyrimidine Stimulating Yeast Fermentation found in the Blood Cells and Urine of Normal Individuals. A. T. Gorham, J. C. Abels, A. L. Robins, and C. P. Rhoads. 161.
The Measurement and Metabolism of Thiamin and of a Pyrimidine Stimulating Yeast Fermentation found in the Blood Cells and Urine of Patients with Leukemia. J. C. Abels, A. T. Gorham, L. Craver, and C. P. Rhoads. 177.
Further Studies on Increased Susceptibility to Chloroform Poisoning produced in the Albino Rat by Injection of Crystalline Thyroxin. M. A. McIver and E. A. Winter. 191.
The Effects of Large Intravenous Infusions on Body Fluid. J. D. Stewart and G. M. Rourke. 197.
Intravenous Magnesium Sulfate in the Treatment of Nephritic Convulsions in Adults. A. W. Winkler, P. K. Smith, and H. E. Hoff. 207.
The Serological Typing of Hemolytic Streptococci of the Lancefield Group A. L. A. Rantz. 217.
Cardiac Output, Blood and Interstitial Fluid Volumes, Total Circulating Serum Protein, and Kidney Function during Cardiac Failure and after Improvement. W. B. Seymour, W. H. Pritchard, L. P. Longley, and J. M. Hayman, Jr. 229.
The Effect of Foreign Surfaces on Blood Coagulation. E. L. Lozner and F. H. L. Taylor. 241.
The Urinary Excretion of Thiamine as an Index of the Nutritional Level: Assessment of the Value of a Test Dose. H. L. Mason and R. D. Williams. 247.

JOURNAL OF COMPARATIVE NEUROLOGY

Vol. 74. No. 3. June 1941.

The Cerebral Cortex of the Penguin. E. H. Craigie. 353.
The Connections of the Basal Optic Root (Posterior Accessory Optic Tract) and its Nucleus in Various Mammals. L. A. Gillilan. 367.
Cerebral Cortical Stimulation of Goats, Normal and Nervous. S. L. Clark, J. W. Ward, and I. S. Dribben. 409.
Further Studies in Naso-Genital Relationship. Anatomical Studies of the Peri-Hypophyseal Region in the Rat. L. R. Zacharias. 421.
Development of the Afferent Components of the Facial, Glosso-pharyngeal and Vagus Nerves in the Rabbit Embryo. D. L. Kimmel. 447.
Development of the Optic Nerves of *Amblystoma*. C. J. Herrick. 473.

Vol. 75. No. 1. August 1941.

The Effect of Crossing Nerves to Antagonistic Muscles in the Hind Limb of the Rat. R. W. Sperry. 1.
Some Reflex Effects of Nerve Crossing and Nerve Regeneration. W. G. Watrous and J. M. D. Olmsted. 21.
The Development of the Nervus Terminalis in Man. A. A. Pearson. 39.
Thalamo-Cortical Connections of the Rat's Brain. K. S. Lashley. 67.
The Vascular Pattern in the Central Nervous System of the Monotremes and Australian Marsupials. S. Sunderland. 123.
Structure of the Area Striata of the Cat. J. L. O'Leary. 131.
The Early Development of the Fascicular Longitudinals Medialis and Associated Secondary Neurons in the Rat, Cat and Man. R. Hhines and W. F. Windle. 165.

Vol. 75. No. 2. October 1941.

The Development of the Olfactory Nerve in Man. A. A. Pearson. 199.
Adrenal Innervation. W. E. MacFarland and H. A. Davenport. 219.
The Ratio of Preganglionic Neurons to Postganglionic Neurons in the Visceral Nervous System. G. A. Wolf. 235.
The Growth of Ependyma. R. Altschul. 245.
The Eyes and Optic Paths of the Catfish, *Ameiurus*. C. J. Herrick. 255.
On Encephalometry. A Preliminary Study of the Brain of Man, Chimpanzee and Macaque. G. von Bonin. 287.
The Ansoparamedian Lobule of the Cerebellum and its Correlation with the Limb-Muscle Masses. O. Larsell and S. von Berthelsdorf. 315.
Spinal Autonomic Outflows in Man and Monkey. D. Sheehan. 341.

Vol. 75. No. 3. December 1941.

Sensory Nerves and Associated Structures in the Skin of Human Fetuses of 8 to 14 weeks of Menstrual Age Correlated with Functional Capability. I. D. Hogg. 371.
The Mammillary Peduncle and Ventral Tegmental Nucleus in the Cat. C. A. Fox. 411.
The Diencephalon of the Coney, *Hyrax Syriaca*. M. Ibrahim and W. M. Shanklin. 427.
Optic and Postoptic Systems of Fibres in the Brain of Necturus. C. J. Herrick. 487.

JOURNAL OF MENTAL SCIENCE

Vol. 88. No. 370. January 1942.

Hyperthyrotic Catatonia: A Schizophrenic Symptom-Complex. R. E. Hemphill. 1.
The Prognostic Factors of Adolescent Psychoses. A. Barham Carter. 31.
Observations in Hypoglycæmia. III. C.S.F. Sugar and Coma. W. Mayer-Gross. 82.
The Treatment of Tuberculosis in Unco-operative Patients. A. Kennedy. 89.
Electro-encephalography in Cases of Mental Disorder. W. G. Walter. 110.
Further Observations on Sodium Amytal Experiments. F. Reitmann. 122.
Blood Amines. D. Richter and M. Lee. 127.
Three Ganser States and Hamlet. E. S. Stern and W. H. Whiles. 134.

Vol. 88. No. 371. April 1942.

The Investigation of Personality in Patients treated by Prefrontal Leucotomy. E. L. Hutton. 275.
Some Preliminary Remarks on Prefrontal Leucotomy. G. W. T. H. Fleming. 282.
Forms of Behaviour of the Electrical Resistance of the Skin related to Certain Psychiatric and Endocrine Conditions. H. E. Hemphill. 285.
The Measurement of Body Resistance by Bridge Methods. W. Grey Walter. 306.
Auxiliary Genes for Determining Sex as Contributory Causes of Mental Illness. L. S. Penrose. 308.
The Measurement of Dementia. M. B. Brody. 317.
Psychiatric Syndromes following Blast. E. W. Anderson. 328.
Arhinencephaly with Incomplete Separation of the Cerebral Hemispheres. G. W. T. H. Fleming and R. M. Norman. 314.

JOURNAL OF NERVOUS AND MENTAL DISEASE

Vol. 94. No. 4. October 1942.

Acute Demyelinizing Processes in the Nervous System. A. J. E. Akelaitis and P. H. Garvey. 405.
Félix Vicq D'Azyr and Benjamin Franklin. R. Spillman. 428.
Huntington's Chorea. H. G. Hadley. 445.
Toxic Psychosis Due to Thiocyanate. M. R. Plesset. 447.
Intracranial Lesions as a Cause of Sudden Death. E. V. Swift, and F. P. Moersch. 452.
A Rorschach Study of Psychotic Personality in Uniovular Twins. G. W. Kisker and N. Michael. 461.

Vol. 94. No. 5. November 1941.

Two Cases of Myelodysplasia. A. Austregesilo and A. R. de Mello. 529.
A Case of Puerperal Psychosis recovering from Four Attacks. H. G. Hadley. 540.
A Study of Migraine. C. T. Gayley. 542.
Complications and Unusual Phenomena arising in the Course of Metrazol Treatment of the Psychoses —Their Classification and Management. J. Epstein. 562.
Angioma Simplex of the Pons. K. T. Neubuerger and W. L. Silcott. 586.
Recent Progress in Psychosomatic Medicine. J. Notkin. 593.

Vol. 94. No. 6. December 1941.

Monstrosity due to Intrauterine Purulent Meningo-Encephalitis. H. N. Roback and H. F. Kahler. 669.
The Challenge of Social Neuroses. W. Eliasberg. 676.
Pneumographic Patterns during Convulsive Therapy of Schizophrenia. E. Friedman and H. Barry. 688.
The Narcoleptic-Cataplectic Syndrome and its Accompanying Mental States. S. Brock and B. Weisel. 700.
Family Periodic Paralysis associated with Exophthalmic Goiter. A. G. Hildebrand and E. J. Kepler. 713.
Epilepsy and Suicide. C. Prudhomme. 722.
Hallucinosis as a Clinical Entity and its Interpretation. A. Gordon. 732.

JOURNAL OF NEUROPATHOLOGY AND PSYCHIATRY, LENINGRAD

Vol. 9. No. 10. 1940.

Tentative Treatment of Atypical and Delayed Alcoholic Psychoses by Hypoglycæmia. Malkin and Yankowsky. 3.
Hepato-Lenticular Degeneration. Konovalov. 12.
Psychic Changes in the Initial Stages of Chronic Mercurial Intoxication. Semenova. 22.
Vegeto-Animal Syndrome in Catatonia. Convulsive Therapy and Dynamics of Chronic Schizophrenia. Karashkevish. 30.
Influence of Shock Therapy on Chronic Schizophrenia. Moskin. 38.
Polyganglio Radiculitis. Luria. 45.
Leydon-Westphal Syndrome in Malaria. Malkich. 51.
Traumatic Ophthalmoplegia. Smynov. 55.
Facial Diplegia in Cranial Injury. Benkovich. 58.
Meningococcal Septicæmia. Strachovich. 62.
Intradermal Therapy and its Mechanism. Birbrayer. 64.
Foreign Bodies in Gastro-Intestinal Tract in the Insane. Smirnov and Gurstev. 65.
Disturbance of Sleep with Bulimia and Polydipsia. Footer. 68.

Vol. 9. No. 12. 1940.

Bilateral Injury of Parietal Cortex. Golandt. 3.
Complex Tactile Kinetic Hallucination (Stereognostic). Ravkin. 14.
Reduced Orientation. Chlenro and Shubert. 25.
Pathological Anatomy of Encephalitis B. Chenisheo and Lukonsky. 30.
Influenzal Psychoses. Yankovsky. 43.
Psychic Changes in Brucellosis. Jekoboo. 49.
Psychogenesis in Early Childhood. Blay. 56.
Organization of Dispensary Psychiatric-legal Investigations. 62.
Action of Morphic Preparations. 68.
Treatment of Endogenous Depressions with Cortin. Korolook. 75.
Treatment of Schizophrenia. Ovchavenko. 78.
Basic Changes in Subdural Insufflation of N_2O and O_2. 81.

Vol. 10. No. 1. 1941.

Founders of Moscow School of Neuropathologists. 3.
Pathogenesis of Epilepsy. Sep. 9.
Theory of Treatment of Schizophrenia. Gurevich. 17.
Convulsive Therapy. Deterof. Magnitzky and Hahativian. 21.
Structure of Psychosis in Insulin Therapy. Zalmarson. 39.
Results of Insulin Therapy, 1937–40. Molokov 44.
Achievements of Soviet Neuropathology. Horoshleo. 52.
Basic Organization in Psychiatric Dispensaries. Karanovich. 57.
Vitamins and the Nervous System. Bron. 67.

Vol. 10. No. 2. 1941.

Role of Vegetative Nervous System in Physiological and Pathological Processes. Proppu-Grashchenko. 5.
Residual Phenomena in Parameningo Encephalitis in the Young. Geyon. 15.
AC. Encephalitis. Perviskin. 21.
Neurological Symptoms in Chronic Sinusitis. Chodoc. 28.
On Anterior External Arcuati and Intra-pyramidal Arcuati Fibres. Fayzoolajer. 41.
Clinical Features of Cerebral Embolism in Organic Heart Disease. Mukeer. 45.
Similarities and Differences in Visual and Auditory Cortex. Blinkov. 48.
Aclinomycosi of Cerebrum. Vizen. 53.
Applications in Painful Irritations in Neuralgias. Choorayev. 55.
Syndrome Unilateral Paralysis, Numerous Cranial Nerves. Hazanov. 59.
Malarial Cerebrospinal Meningitis. Malkiel. 61.
On Unequal Pupils. Smirnov. 64.
Cerebral Injury. Duchinsky. 68.
Diencephalic Epilepsy and its Treatment. Veinberg. 72.
Epilepsy as a Reflex to Physiological Irritation. Yesclavich. 74.
Prevention of Contractures in Nervous Affections of the Central Nervous System. Shiform and Horavkin. 76.
Certain Pathological Changes in Nervous System in Hydrophobia. Uspensky. 79.
Mitogenic Rays in C.S.F. in Affections of Nervous System. Lotzman. 81.
Complications of Epidemic Meningitis in Children. Shirokov. 84.
Case of Relapsing Myelitis Gravidarum Toxica. Maximov. 86.
Three Cases of Affections of the Nervous System by Lightning. Shendetovich. 86.
Treatment of Injury of Spinal Cord. Karaev and Fooki. 89.
Catheterization of the Sylvian Aqueduct. Yoselevich. 90.
Amyostatic Symptom-complex in a Case of Kayser Fleisher Ring occurring in Familial Disease simulating Banti's Disease. Shternberg. 92.
Extrapyramidal Symptoms in Tumours of the Cerebello-pontine Angle. Litvak. 95.
Supracellar Tumours. Mazilo. 96.
Magnesium and Calcium in the Cerebrospinal Fluid and in Blood Serum in Nervous Diseases. Pleshchitser. 98.
Radiological Investigations of the Cardiovascular and Respiratory Systems in the Insane. Kosliki and Goldberg. 99.
Quiet as a Therapeutic Agent in Noisy Patients. Kliptsan. 103.
Decentralization of Psychiatric Help. Berger. 105.

Vol. 10. No. 3. 1941.

Work of Professor Osipov. Zuzin. 3.
Genesis of Affective States. Osipov. 7.
Carriers and Reservoirs in Virus of Encephalitis. Pavlovski. 10.
Therapy of Nervous Diseases. Davidenko. 12.
Diencephalopathic Psychoses of Periodicity. Golant. 18.
Ontogenesis of Vegetative Centres in Humans. Piness. 24.
Character of Berger Rhythm in Normal and Pathological Cases. Sarkisov and Livranov. 28.
Influence of Cerebellum and Cerebrum on the Vegetative Functions. Asrotyn. 35.
Traumatic Epilepsy. Omorokov. 39.
Re-establishment of Suppressed Functions. Vasiliev. 44.
Individual Differences in Sensitiveness. Aranyev. 49.
Theory of Hallucinations. Rorchevsky. 53.
Histopathology of Hepato Lenticular Degeneration. Konovalov. 59.
Non-specific Therapy in Epidemic Cerebrospinal Meningitis. Alexandrov. 67.
Nervous Syndrome in Infectious "Nephrosis." Shapoval. 70.
Spring-Summer Encephalitis. 1939. Arbuzov. 73.
Alternative Clonus of Big Toe. Lichtenstein. 77.
High Frequency Currents in Affections of the Peripheral Nerves. Kovda. 82.
Research on Chronaxie in Demyelinated Nerves. Ignatov and Feldman. 88.

JOURNAL OF NEUROPHYSIOLOGY

Vol. 4. No. 5. July 1941.

Cerebral Blood Flow and *p*H in Excessive Cortical Discharge induced by Metrazol and Electrical Stimulation. H. Jasper and T. C. Erickson. 333.
Relation between Electrical Changes during Nerve Activity and Concentration of Choline Esterase. D. Nachmansohn and B. Meyerhof. 348.
*Nature of the "Endplate Potential" in Curarized Muscle. J. C. Eccles, B. Katz, and S. W. Kuffler. 362.
*Isolation of Intrinsic and Motor Mechanism of the Monkey's Spinal Cord. S. Tower, D. Bodian, and H. Howe. 388.
*Fibrillation in Skeletal Musel in Relation to Denervation and to Inactivation without Denervation. S. Tower, H. Howe, and D. Bodian. 398.
*Initiation of Muscle Impulses at Neuro-Muscular Junction. J. C. Eccles and S. W. Kuffler. 402.
*The Human Electro-Corticogram. J. E. Scarff and W. E. Rahm. 418.

Cerebral Blood Flow and *p*H in Cortical Discharge.—Local increased acidity of the cortex resulting from neuronal discharge causes a vascular dilatation which tends to maintain a constant *p*H. Thus relative acidity caused by a metrazol discharge is followed by a relative alkalinity as blood flow is increased. It is suggested that small

alkaline waves concomitant with onset of facilitation may be due to DC voltage components of the cortical electrogram in a violent metrazol discharge. The features of the metrazol discharge are not altered by variations in *p*H of the cortex between 7·0 and 7·5 induced by hyperventilation, CO_2 and injection of acid or alkaline solutions into the blood stream. After discharge induced by contralateral cortical impulses shows local cortical *p*H and blood flow changes similar to those of a metrazol discharge. It is concluded that increase in *p*H is a result of vascular reaction to increased neuronal activity and is not important in facilitation processes. (W. M. H.)

"**Endplate Potential.**"—The endplate potential (e.p.p.) set up by a nerve volley at the region of the myoneural junction is shown to be a local depolarization of the muscle fibres acting like a local catelectrotonic potential produced by a subthreshold electric stimulus. It spreads a short distance along the muscle fibres with considerable decrement and progressive slowing. The time course of its waning phase is little altered by heat in contrast with the rising phase. In the frog a second nerve volley sets up an e.p.p. which is 80–100 per cent. larger than the first. Muscle spikes are initiated when e.p.p. reaches a certain critical level. Neuromuscular facilitation occurs when the required level is reached by summation of successive e.p.p.'s. (W. M. H.)

Isolation of Intrinsic Mechanism of Spinal Cord.—In two monkeys a study was made of the lumbo-sacral cord 10–14 days after complete transection at the last thoracic segment, and section of all the posterior roots. Thus it was possible to view the intrinsic and motor mechanism of the spinal cord cleared of all descending and posterior root fibres. In such a condition the skeletal muscle is wholly inactive. (W. M. H.)

Fibrillation in Skeletal Muscle.—In a preparation such as the preceding fibrillation is observed in leg muscles only if the sciatic nerve is cut. Atrophy developing in conditions of inactivation without denervation may thus properly be considered atrophy of disuse. (W. M. H.)

Initiation of Impulses at Neuro-Muscular Junction.—The rising phase of the muscle action potential set up at a focus of endplates by a nerve volley is shown to have a component due to endplate potential (e.p.p.), the initial step of the potential of normal muscle allowing of matching by the e.p.p. seen in curarized muscle. Simple spike and double stop types of action potential differ only in the time of the spike origin relative to the e.p.p. In the latter the spike arises only when the e.p.p. has reached 16 per cent. of the peak potential. Large initial e.p.p.'s (12–18 per cent.) are probably the sole mechanism initiating muscle impulses normally and in sub-paralytic curarization ; where initial e.p.p.'s are small an additional excitatory mechanism, possibly nerve action currents, forestalls the excitatory action of the e.p.p. (W. M. H.)

Human Electro-Corticogram.—A compact apparatus is described for the recording of electrical potentials of the brain exposed at operation. Findings in abnormal conditions are given. (W. M. H.)

Vol. 4. No. 6. September 1941.

Effect of Chronic Painful Lesions on Dorsal Root Reflexes in Dog. R. Anderson, W. K. Livingston, and R. S. Dow. 427.
*Reflex Activity in the Spinal Extensors. J. S. Denslow and G. H. Clough. 430.
*Steady Potential Fields and Neurone Activity. B. Libet and R. W. Gerard. 438.
*Fatigue and Refractoriness in Nerve. E. T. von Brücke, M. Early, and A. Forbes. 456.
*Acetylcholine Esterase Concentration during the Development of the Human Fetus. K. A. Youngstrom. 473.
*Localization of Cerebral Center Activating Heat-Loss Mechanisms in Monkeys. L. E. Beaton, W. A. McKinley, C. M. Berry, and S. R. Ranson. 478.
*The Endplate Potential during and after the Muscle Spike Potential. J. C. Eccles and S. W. Kuffler. 486.

Reflex Activity in Spinal Extensors.—Cases of periarticular disease showing no obvious organic pathology nor voluntary muscle contraction were examined for abnormal muscle activity in the segments of the lesion. Activity in motor units were sometimes found when the subject was at rest. The rate of unit discharge was 3–24 per sec. The origin of these reflex discharges is thought to be in abnormal stresses in joints. (W. M. H.)

Steady Potential Fields and Neurone Activity.—The passage of potential waves through the cerebral hemispheres after neural connections are blocked depends on inter-cellular currents. These are considered to come from a potential from the axonic to dendritic pole of similarly oriented neurones. Inter-cellular currents may be of importance in the synchronizing of neurones and the mass functioning of the cortex. Steady potentials between the pial and ventricular surfaces of the frog's brain, caffeine potential waves and the effect of depolarization at points in the hemisphere are here described. (W. M. H.)

Fatigue and Refractoriness in Nerve.—The effect of prolonged repetitive stimulation of medullated nerve is to delay recovery of responsiveness (size of maximal response) in the relative refractory phase and, to a greater extent, recovery of

excitability. Excitability is reduced much more in the unconditioned (resting) than in the conditioned (refractory) nerve. Separate refractory states after two impulses are shown to sum in the same way as subnormality. Subnormality, the relatively slow recovery of excitability, is regarded as a continuation of the relative refractory state, during which responsiveness is recovered. (W. M. H.)

Acetylcholine Esterase Concentration during Human Fetus Development.—The periods of increase of choline esterase in the various parts of the nervous system of the human fœtus follows the order of their morphological differentiation (midbrain and medulla, spinal cord, diencephalon, basal ganglia, and cerebral hemispheres). The most rapid concentration of the esterase in muscles of the shoulder girdle occurs when motility is developing (about 80 days). (W. M. H.)

Heat-Loss Mechanisms in Monkeys.—With the Horsley Clarke technique in monkeys an area in the preoptic region is shown on heating with a low voltage, high-frequency current to cause sweating and polypnœa. A similar local control of the heat-loss mechanism is likely in man. (W. M. H.)

Endplate and Muscle Spike Potentials.—The difference between the anti-dromic spike potential set up by direct stimulation and the potential when a nerve volley is added, gives the size of e.p.p. during and after the muscle spike potential. Sub-paralytic curarization diminishes the size and shortens the duration of e.p.p. Also in refractory muscle e.p.p. decays more rapidly than in the normal. In the cat e.p.p. co-existing with the muscle spike (i) prolongs the refractory period, lengthening by 0·8 m. sec. the least spike interval for a testing nerve volley, and (ii) raises the threshold level of e.p.p. for initiating a spike. (W. M. H.)

Vol. 4. No. 7. November 1941.

On the Alleged Synchronization of Proprioceptive Impulses within Spinal Ganglia. E. Th. von Brücke and M. Early. 507.
*Hyperactivity in Monkeys following Lesions of the Frontal Lobes. M. A. Kennard, S. Spencer, and G. Fountain. 512.
*The Spinal Mechanism of the Pyramidal System in Cats. D. P. C. Lloyd. 525.
Crossed Inhibition of the Flexor Reflex in the Spinal Mammal. G. P. McCough, J. Hughes, and W. B. Stewart. 547.
Cortical Origin and Distribution of Corpus Callosum and Anterior Commissure in the Monkey (*Macaca mulatta*). W. S. McCulloch and H. W. Garol. 555.
Cortical Origin and Distribution of Corpus Callosum and Anterior Commissure in Chimpanzee (*Pan satyrus*). P. Bailey, H. W. Garol, and W. S. McCulloch. 564.
Potassium and Water Changes in Excised Nerve on Stimulation. V. Arnett and W. S. Wilde. 572.

Hyperactivity following Frontal Lobe Lesions.—In monkeys and chimpanzees ablation of the frontal association areas (8–12 of Brodmann) cause greatly increased total activity. This hyperactivity is purposeless and repetitious. It is dependent on vision, disappearing in the dark, after eneucleation of the eyes and occipital lobectomy. Hypomotility is related to lesions of the rostral parts of areas 6 and of area 8. (W. M. H.)

Spinal Mechanism of Pyramidal System.—Stimulating the pyramidal fibres in the medulla of the cat the authors have studied the working of the spinal interneurons in the relay of pyramidal activity. Small nuclear elements close to the tract are the initial, the cells of the intermediate region the premotoneuron relay. Facilitation of motoneurons as tested through primary afferent volleys parallels activity in the intermediate region. As pyramidal activity is intensified, shortening of the functional path to the motoneurons occurs. Reciprocal innervation is accounted for by inhibition of some interneurons of the intermediate region. Motoneuron discharge from pyramidal activity is highly asynchronous. Spinal reflex reinforcement of pyramidal activity begins with the onset of movement. (W. M. H.)

JOURNAL OF PHYSIOLOGY

Vol. 100. No. 3. November 1941.

The Ratio between Antidiuretic and Pressor Activities of Posterior Pituitary Extract subjected to Mild Hydrolysis. A. M. Fraser. 233.
A Method for Estimating the Fraction of the Volume of a Muscle contained in the Vascular System. J. F. Danielli. 239.
The Volume of the Vascular System, and Penetration of Sugars from the Vascular System into the Intercellular Space. J. F. Danielli and H. Davson. 246.
An Investigation of Simple Methods for Diagnosing Vitamin A Deficiency by Measurements of Dark Adaptation. D. J. Dow and D. M. Steven. 256.
The Behaviour of the Pregnant Uterus of the Guinea Pig. G. H. Bell. 263.
A Quantitative Method of Assay for Thrombin and Prothrombin. L. B. Jaques. 274.
*The Latency and Conduction of Potentials in the Spinal Cord of the Frog. Fwu Tarng Dun. 282.
Strength and Size of Bone in Relation to Calcium Intake. G. H. Bell, D. P. Cuthbertson, and J. Orr. 298.
*Abortive Impulses at the Neuro-Muscular Junction. J. C. Eccles and W. J. O'Connor. 317.
The Glycogen Content of the Frog's Heart. F. Davies and E. T. B. Francis. 328.
*Observations Bearing on Synaptic Transmission by Acetylcholine in the Spinal Cord. E. Bülbring and J. H. Burn. 336.

Latency and Conduction of Spinal Cord Potentials.—When a volley of sensory impulses is sent into the spinal cord potential changes may be detected in the ipsilateral and some contralateral dorsal roots. The latency of this dorsal root potential increases with the distance between the roots of stimulation and observation. It does not vary with change in the intensity of stimulation. The potential seems to depend on the integrity of the dorsal columns and is conducted at 1–2 m./sec. The potential is considered to arise presynaptically and excitation of secondary neurones to occur during its rising phase. (W. M. H.

Abortive Impulses at Neuro-Muscular Junction.—At the endplate region of cats' solens abortive impulses spreading less than 1 mm. are observed on curarization in the refractory state of neuro-muscular transmission. It is shown that the endplate potential set up in normal muscle by an early second volley is diminished to one-third by refractoriness. With increasing volley interval the action potential of the second becomes steeper and greater till an inflexion on the rising phase shows the spike due to a fully propagated muscle impulse. With longer volley intervals the spike origin encroaches progressively earlier on the e.p.p. These observations on the role of e.p.p. in the rising phase of the action potential necessitate a revision of earlier views. (W. M. H.)

Synaptic Transmission by Acetylcholine.—Acetylcholine injected into the cord circulation in the dog has a transient depressant effect on the knee jerk. It augments the flexor reflex slightly. Eserine, prostigmine, and nicotine all depress the knee jerk and augment the flexor reflex. After eserine and prostigmine acetylcholine depresses or abolishes the knee jerk. After eserine the inhibition of the knee jerk caused by stimulation of the posterior tibial nerve is followed by an exaggerated rebound. The effects of acetylcholine are considered to resemble those of posterior tibial nerve stimulation, both before and after eserine. After stimulation of the central end of the cut sciatic nerve acetylcholine is found in the venous effluent from the cord if Ringer's solution containing eserine be used. Adrenaline facilitates the discharge of impulses from the spinal cord following the injection of acetylcholine. (W. M. H.)

PHYSIOLOGICAL REVIEWS

Vol. 21. No. 3. July 1941.

Endocrines in Invertebrates. B. Scharrer. 383.
Organic Acid-Soluble Phosphorus Compounds of the Blood. G. M. Guest and S. Rapaport. 410.
The Nutrition of the Fetus. A. St. C. Huggett. 438.
The Circulation of the Bile Acids in Connection with their Production, Conjugation and Excretion. B. Josephson. 463.
The Physiology of the Gene. S. Wright. 487.

Vol. 100. No. 4. March 1942.

A Note on Interaction between Nerve Fibres. B. Katz and O. H. Schmitt. 369.
The Assimilation of Radio-active Phosphorus Deficiency in Rats. W. E. Gaunt, H. D. Griffith, and J. T. Irving. 372.
Glycogen and Adipose Tissue. E. Tuerkischer and E. Wertheimer. 385.
Ovulation in the Rabbit after Destruction of the Greater Superficial Petrosal Nerves. M. Vogt. 410.
The Action of Curare on the Respiratory Centre. J. Fegler. 417.
The Influence of a Deficiency of Vitamin B_1 and of Riboflavin on the Reproduction of the Rat. K. H. Coward, B. G. E. Morgan, and L. Waller. 423.
Urea Formation in the Isolated Perfused Liver of the Rat. O. A. Trowell. 432.
*Olfactory Reactions in the Brain of the Hedgehog. E. D. Adrian. 459.
*Observations on the Properties of S-methyl Iso-Thiourea Sulphate, with Particular Reference to the Circulatory Effects. M. McGeorge, M. Sherif, and F. H. Smirk. 474.

Olfactory Reactions in Brain.—In the hedgehog electrical activity in the olfactory bulb and olfactory area of the brain has been studied in nembutal and chloralose anæsthesia. Normal breathing produces at each inspiration a regular series of large potential waves of frequency about 15 p. sec. Forcible sucking of air through the snout increases the frequency to 45 p. sec. Small irregular waves replace these regular waves when a distinct odour is added to the air. It is suggested that the olfactory organ may be stimulated mechanically by the air current as well as chemically by the odours in it, and that different chemical stimuli produce different distributions of excitation and so different patterns in the brain. (W. M. H.)

Circulatory Effects with S-Methyl Iso-Thiourea Sulphate.—In the anæsthetized decerebrate and pithed animal S-methyl iso-thiourea sulphate produces a considerable and prolonged rise in blood pressure, accompanied by some slowing of the heart. The rise in B.P. is found after blocking of sympathetic motor nerve endings by either ergotamine or F 933, and the slowing of the heart is independent of the vagus. Study of the relative effect of like concentrations in the whole animal and isolated heart indicates that the substance undergoes a change in composition in the whole animal. (W. M. H.)

Vol. 21. No. 4. October 1941.

Factors affecting the Tests of Kidney Function. R. C. Herrin. 529.

Anaphylaxis. C. A. Dragstedt. 563.
Antihormones. K. W. Thompson. 588.

Vol. 22. No. 1. January 1942.

The Insensible Loss of Water. L. H. Newburgh and M. W. Johnston. 1.
Hemoglobinuria. C. L. Yuile. 19.
The Fuel for Muscular Exercise. C. L. Genmill. 32.

Recent Advances in Knowledge of the Liver. C. D. Snyder. 59.
The Present Status of the Shock Problem. C. J. Wiggers. 74.

PSYCHIATRIC QUARTERLY

Vol. 16. No. 1. January 1942.

The Rorschach Method and Its Uses in Military Psychiatry. J. A. Brussel and K. S. Hitch. 3.
A Comparative Table of the Main Rorschach Symbols. Z. A. Piotrowski. 30.
The Catatonic Death Reaction. P. Milici. 38.
Some Shakespearean Characters in the Light of Present-Day Psychologies. I. S. Wile. 62.
Alzheimer's Disease. W. H. English. 91.
Problems of Cancer Therapy in a State Hospital. J. Moore. 107.
The Validity of the Shipley-Hartford Retreat Test for "Deterioration." B. Pollack. 119.
Juvenile Amaurotic Idiocy. G. A. Jervus, L. Roizin, and W. H. English. 132.

Family Care Placement of State Hospital Patients as a Method of Situational Therapy. K. Stuber and H. B. De Witt. 144.
Echo of Reading: Impersonal Projection in Schizophrenia. M. C. Meehan. 156.
Ambulatory Insulin Therapy. P. J. Tomlinson and L. D. Ozarin. 167.
Varicella with Encephalitis. S. C. Karlan. 174.
The Incidence of Psychoses and Other Mental Abnormalities in the Families of Recovered and Deteriorated Schizophrenic Patients. O. Kant. 176.
Adolf Hitler's "My New Order"—A Critical Review. 187.

Vol. 16. No. 2. April 1942.

Anxiety in a Neurosis of 70 Years' Standing. C. P. Oberndorf and A. Eisendorfer. 221.
Folie a Deux—the Psychosis of Association. A. Gralnick. 230.
Mental Defectiveness with Unusual Syndrome of Congenital Physical Anomalies. S. Androp. 264.
Deeper Level of Regression. G. S. Sprague. 272.
Hirsutism. J. H. Schwartz. 281.
Review of the Research Program of the New York State Psychiatric Institute and Hospital for 1941. N. D. C. Lewis. 295.
A 10-Year Comparative Study of the Treatment of General Paresis with Fever Therapy (Radiant Energy) and Chemotherapy. K. K. Slaght and N. Jones. 306.
Preliminary Study of the Art Productions of the Adult Psychotic. J. Zimmerman and L. Garfinkle. 313.

Massive Dose Testosterone Therapy in Male Involutional Psychosis. M. Zeifert. 319.
Treatment of Speech Defects in a State Schooi. J. Sirkin and W. F. Lyons. 333.
The Problem of Psychogenic Precipitation in Schizophrenia. O. Kant. 341.
Asphyxial Episodes and their Prevention in Electric and other Convulsive Therapies. H. Brill and L. Kalinowsky. 351.
Progressive Lenticular Degeneration. G. A. Jervis, J. Notkin, I. S. Freiman, and J. Moore. 357.
Without Psychosis—Chronic Alcoholism. C. A. Whitaker. 373.
Reducing the State Hospital Population. W. A. Thompson. 393.
Experience with Intravenous Use of Solution of Crystalline Zinc-Insulin in the Hypoglycemic Treatment of Schizophrenia. L. Reznikoff and J. J. Scott. 399.

SCHWEIZER ARCHIV FÜR NEUROLOGIE UND PSYCHIATRIE

Vol. 48. No. 1. 1941.

L'Amnesia retrograda dopo l'Elettroshock. Contributo allo studio della patogenesi delle amnesie in genere. (Retrograde amnesia in electrically induced convulsions. A contribution to the study of the pathogenesis of amnesia.) G. Flescher. 1.

Spiegelschrift bei Triebstö rungen. (Mirror-writing in disturbances of instinctive reactions.) K. Heymann. 29.

A propos de la classification des tumeurs cérébrales. (Classification of cerebral tumours.) M. Jequier-Doge. 40.

Zur Kritik des Typenbegriffes. (A criticism of the doctrine of "types.") R. Meili. 71.

Un cas de polyradiculo-névrite ascendante subaiguë avec dissociation albumino-cytologique. Étude anatomoclinique. (Ascending polyradiculoneuritis with cyto-albuminous dissociation. A patholoclinical and anatomical study.) T. Ott. 83.

Uber Möglichkeiten artgleicher Normalserumbehandlung als Sukkurstherapie. (The experimental use of normal serum as a therapeutic adjunct.) E. Stransky. 106.

Schizophrenie bei eineiigen Zwillingen. Kasuistischer Bericht zum Problem "endogen-exogen" in der Schizophrenieforschung. (Schizophrenia in uniovular twins. The problem of endogenous *v.* exogenous in the causation of schizophrenia.) H. Wespi. 110.

Sitzungsberichte—Comptes rendus des séances: Comptes rendus de la XLVIII[e] Assemblé de la Société Suisse de Neurologie, à Berne, les 7 et 8 décembre, 1940. (Transactions of the 48th meeting of the Swiss Neurological Society at Berne, December 7th and 8th, 1940.) 129.

BOOK REVIEWS

BACTERIOLOGY IN NEUROPSYCHIATRY

Nicholas Kopeloff, Ph.D.

(Springfield and Baltimore Charles C. Thomas. 1941. Pp. 316. 25*s*.)

The subject-matter of this book deals with bacteriological and immunological aspects of diseases of known and of unknown ætiology and with primary and secondary involvement of the nervous system in the group of diseases of known causation. Many of this last group are of little interest to the neurologist or the psychiatrist, and some space is also used in quoting references to delirium in association with a large variety of diseases discussed.

The author gives a short, even in some cases scanty, description of the causal organism if such exists, with the pathology and experimental work relating thereto, and the symptoms and treatment of each disease discussed. Most of the experimental work referred to is recent and a large proportion of it is from American workers.

The conclusions reached in the part relating to mental disorders is almost entirely of a negative nature, but this is hardly surprising in view of the degree of reliability of the work discussed.

A portion of the book is devoted to such conditions as anaphylaxis, serum sickness, and allergy, and it is suggested that allergy may play some part in migraine.

As a whole the book is rather disappointing to the bacteriologist and even to the neurologist, as its title leads one to believe that bacteriology will be the dominant feature. A reasonably exhaustive and useful series of references is given.

AN INVESTIGATION OF THE TECHNIQUE OF PSYCHO-ANALYSIS

Edward Glover, with the assistance of Marjorie Brierley

(Baillière, Tindall, and Cox, London. 1940. Pp. 188. 10*s*. 6*d*.)

This candid book was compiled from the answers sent by twenty-four practising psycho-analysts to a series of questions asking them details of their technique. Technique in psycho-analysis goes hand in hand with theory, on which the members of this group would in the main be in agreement, yet the report here presented shows how diverse was their procedure. On the interpretation of material presented by the patient there are four illuminating chapters; the attitude of the analyst and his ways of influencing the relationship between himself and the patient are dealt with in two further chapters on "Transference and Routine." Other topics are the indications for terminating the analysis, the criteria of success, methods used for analyzing the insane, and the relation of theory to practice: appendices give the questionnaires used and the condensed outcome of the inquiry.

Useful as this inquiry may be to psycho-analysts, its value is by no means small to those who only read the literature of the subject and hear the views of adherents to the Freudian school, since it enables them to get some idea of the workshops in which the Freudian theories and observations are arrived at, and gives them a chance to appraise the validity of such methods.

SHELL SHOCK IN FRANCE 1914–18

Charles S. Myers

(Cambridge University Press, Cambridge. 1940. Pp. 146. 4*s*. 6*d*.)

This little book contains two chapters on the nature and treatment of neuroses in soldiers, and an account of the problems Dr. Myers met when advising on the administrative steps necessary for dealing with such illness in France and at home. A feeling of frustrated effort is perceptible in the personal part of the narrative.

THE COLLECTED PAPERS OF WILFRED TROTTER, F.R.S.

(Oxford University Press. 1941. Pp. 194. 10*s*. 6*d*.)

Philosophy has been defined as the study of all knowledge with the object of discovering unities and principles common to every branch of human endeavour, common to all man's attempts to understand himself and his environment (including the minute analyses that science makes). It may further attempt to discover a meaning in natural phenomena. When undertaken by professional philosophers the results do not always or even often, add to the understanding of such principles, since the professional begins by studying the ancient systems, with many elisions and compressions of a body of knowledge too vast already for any man's complete assimilation. Trained in a world of ideas he can scarcely produce or teach anything but abstractions. For this reason it is possible that the only admissible philosophers of the future will be those who have received a thorough and practical training in science in one of its forms. Training in the arts and æsthetics is a less permissible portal of entry since these belong more clearly to psychology, so far as they have commerce with anything else. The plain fact is that a great quantity of philosophy is completely out of date and in need of vigorous pruning. This is a really urgent need. It is significant that the most important philosophical contributions of the last two decades have been of the applied kind (Whitehead, Bertrand Russell, Sherrington). It would be too much to expect that all the contributions of an applied type should be first-rate; some of the philosophy that has come recently from the pens of our biologists is undistinguished.

These essays of Wilfred Trotter's are the most important contributions to what we may for the moment term "applied philosophy," and indeed three of them (Nos. 7, 9, and 10) seem to the present writer to be the most penetrating that anybody has written. By his too early death we have lost further and deeper incursions into the realms of pure or professional philosophy. He has already given indications which should influence its course, when the import of his message becomes widely known. Trotter's main contentions concern the fallibility of the mind, of the intellect as a reasoning instrument. Reason can propound a philosophy such as Berkeley's which cannot be disproved but which common sense will always reject. Trotter in his essays uses the modernized language of philosophy. Anyone accustomed to reading philosophy will immediately recognize that the manner of presentation and argument is exactly that of the professional philosopher. He will be grateful for two qualities very uncommon elsewhere, the extreme clarity of the writing and its conciseness. The simplicity and gracefulness of the diction hide the difficulty of the thought expressed.

The finality of these essays is astonishing and amongst the most important is his judgment of the place of medicine in the scientific hierarchy. His criticism of the scientific attitude, of the fallacies latent in philosophic doubt and suspended judgment, is masterly and provides memorable passages. He finds reason to criticize the methods of science itself, without in any sense belittling its achievements. Whitehead had on an even more comprehensive scale done much the same with perfect justice.

Speculation was highly valued by Trotter, though these papers must be carefully read to get the author's exact estimation of it. It is interesting, however, to observe that the only insecure parts in Trotter's own scientific work proved to be in the speculative sphere (e.g. his theory of concussion). We can imagine that he would have accepted the correction with tolerance, for who knew or exposed better than he the infirmities of the intellect, the insecurity of the Reason so beloved by Descartes, Berkeley, Kant, and so many philosophers, earlier and later. His last essay on this subject should become a classic, not only because of its subject-matter but for the beauty of its presentation.

This book will probably appeal less to the young than to their seniors. The former will be deceived by the apparent casualness and obviousness of the themes, which hide so great an intellectual achievement. But the older will ask themselves where they can read the like again and regret the impossibility.

PRINTED IN GREAT BRITAIN BY WILLIAM CLOWES AND SONS, LIMITED, LONDON AND BECCLES.

ST. ANDREW'S HOSPITAL

FOR NERVOUS AND MENTAL DISORDERS

AT NORTHAMPTON

FOR THE UPPER AND MIDDLE CLASSES ONLY

President—The Most Hon. the MARQUESS OF EXETER, K.G., C.M.G., A.D.C.
Medical Superintendent: Thomas Treasurer; J.D., F.R.C.P., D.P.H., D.P.M.

THIS Registered Hospital is situated in 150 acres of park and pleasure grounds. Voluntary patients, who are suffering from incipient mental disorders or who wish to prevent recurrent attacks of mental trouble; temporary patients, and certified patients of both sexes are received for treatment. Careful clinical, bio-chemical, bacteriological, and pathological examinations. Private rooms with special nurses, male or female, in the Hospital or in one of the numerous villas in the grounds of the various branches can be provided.

WANTAGE HOUSE

This is a Hospital Hospital, in detached grounds, with a separate entrance to which patients can be admitted. It is equipped with all the apparatus for the complete investigation and treatment of Mental and Nervous Disorders by the most modern methods; insulin treatment is available for suitable cases. It contains special departments for hydrotherapy by various methods, including Turkish and Russian baths, the prolonged immersion bath, Vichy Douche, Scotch Douche, Electrical baths, Plombières treatment, etc. There is an Operating Theatre, a Dental Surgery, an X-Ray Room, an Ultra-Violet Apparatus, and a Department for Diathermy and High-Frequency treatment. It also contains Laboratories for bio-chemical, bacteriological, and pathological research. Psychotherapeutic treatment is employed when indicated.

MOULTON PARK

Two miles from the Main Hospital there are several branch establishments and villas situated in a park and farm of 330 acres. Milk, meat, fruit and vegetables are supplied to the Hospital from the farm, gardens and orchards of Moulton Park. Occupational therapy is a feature of this Branch, and patients are given every facility for occupying themselves in farming, gardening and hay-making.

BRYN-Y-NEUADD HALL

The Seaside house of St. Andrew's Hospital is beautifully situated in a Park of 330 acres, at Llanfairfechan, amidst the finest scenery in North Wales. On the North-West side of the estate a mile of sea-coast forms the boundary. Patients may visit this Branch for a short seaside change or for longer periods. The Hospital has its own private bathing house on the seashore. There is trout-fishing in the park.

At all the branches of the Hospital there are cricket grounds, football and hockey grounds, lawn tennis courts (grass and hard courts), croquet grounds, golf courses and bowling greens. Ladies and gentlemen have their own gardens, and facilities are provided for handicrafts, such as carpentry, etc.

For terms and further particulars apply to the Medical Superintendent (TELEPHONE Nos. [illegible] Northampton), who can be seen in London by appointment.